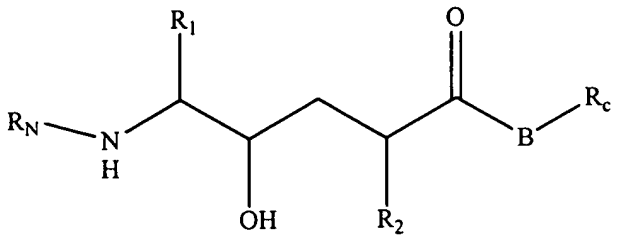
WE CLAIM:

1. A method for inhibiting β-secretase activity, comprising exposing said β-secretase to an effective inhibitory amount of a hydroxyethylene compound of the formula



(XII)

where R_1 is:

(I) C_1-C_6 alkyl, unsubstituted or substituted with one, two or three C_1-C_3 alkyl, –F, -Cl, -Br, -I, -OH, $-NH_2$, -C≡N, $-CF_3$, or $-N_3$,

(II) $-(CH_2)_{1-2}$-S-CH_3,

(III) $-CH_2$-CH_2-S-CH_3,

(IV) -CH_2-(C_2-C_6 alkenyl) unsubstituted or substituted by one –F,

(V) -$(CH_2)_{0-3}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:

(A) C_1-C_3 alkyl,

(B) $-CF_3$,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) –O-CF_3,

(F) $-NH_2$,

(G) -OH, or

(H) -C≡N,

(VI) -$(CH_2)_{n1}$-($R_{1\text{-heteroaryl}}$) where n_1 is 0, 1, 2, or 3 and $R_{1\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{1\text{-heteroaryl}}$ group is bonded to $-(CH_2)_{0\text{-}3}-$ by any ring atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_3 alkyl,

(2) $-CF_3$,

(3) -F, Cl, -Br, or –I,

(4) C_1-C_3 alkoxy,

(5) $-O-CF_3$,

(6) $-NH_2$,

(7) -OH, or

(8) $-C\equiv N$,

with the proviso that when n_1 is zero $R_{1\text{-heteroaryl}}$ is not bonded to the carbon chain by nitrogen, or

(VII) $-(CH_2)_{n1}-(R_{1\text{-heterocycle}})$ where n_1 is as defined above and

$R_{1\text{-heterocycle}}$ is:

(A) morpholinyl,

(B) thiomorpholinyl,

(C) thiomorpholinyl S-oxide,

(D) thiomorpholinyl S,S-dioxide,

(E) piperazinyl,

(F) homopiperazinyl,

(G) pyrrolidinyl,

(H) pyrrolinyl,

(I) tetrahydropyranyl,

(J) piperidinyl,

(K) tetrahydrofuranyl, or

(L) tetrahydrothiophenyl,

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

(1) =O,

(2) C_1-C_3 alkyl,

(3) $-CF_3$,

(4) -F, Cl, -Br and –I,

(5) C_1-C_3 alkoxy,

(6) $-O-CF_3$,

(7) $-NH_2$,

(8) -OH, or

(9) -C≡N,

with the proviso that when n_1 is zero $R_{1\text{-heterocycle}}$ is not bonded to the carbon chain by nitrogen;

where R_2 is:

(I) -H,

(II) C_1-C_6 alkyl, or

(III) -$(CH_2)_{0-4}$-R_{2-1} where R_{2-1} is (C_3-C_6)cycloalkyl, $R_{1\text{-aryl}}$ or $R_{1\text{-heteroaryl}}$ where $R_{1\text{-aryl}}$ and $R_{1\text{-heteroaryl}}$ are as defined above,

where R_N is:

(I) R_{N-1}-X_N- where X_N is:

(A) –CO-,

(B) –SO_2-,

(C) -$(CR'R'')_{1-6}$ where R' and R" are the same or different and are –H or C_1-C_4 alkyl,

(D) –CO-$(CR'R'')_{1-6}$-X_{N-1} where X_{N-1} is –O-, -S- and –NR'R"- and where R' and R" are as defined above,

(E) a single bond;

where R_{N-1} is:

(A) $R_{N\text{-aryl}}$ where $R_{N\text{-aryl}}$ is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or -I,

(3) -OH,

(4) -NO_2,

(5) -CO-OH,

(6) -C≡N,

(7) -CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) $-C_1$-C_6 alkyl unsubstituted or substituted with one to three –F, -Cl, -Br, or -I,

(d) $-C_3$-C_7 cycloalkyl,

(e) $-(C_1$-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) $-(C_1$-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) $-C_1$-C_6 alkenyl with one or two double bonds,

(h) $-C_1$-C_6 alkynyl with one or two triple bonds,

(i) $-C_1$-C_6 alkyl chain with one double bond and one triple bond,

(j) $-R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) $-R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) $-CO-R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) $-CO-R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) $-CO-R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) $-CO-O-R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) $-(CH_2)_{0\text{-}2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) $-SO_2-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) $-SO_2$-(C_3-C_{12} alkyl),

(17) $-NH-CO-O-R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(18) $-NH-CO-N(C_1$-C_3 alkyl)$_2$,

(19) $-N-CS-N(C_1$-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-R_{N-5} where R_{N-5} is as defined above,

(21) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(22) -R_{N-4} where R_{N-4} is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH,

(28) -S-(C_1-C_6 alkyl),

(29) C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F,

(30) –O-(C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F, or

(31) –O-ϕ,

(B) -$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{N\text{-heteroaryl}}$ group is bonded by any atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{N\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or - I,

(3) -OH,

(4) $-NO_2$,

(5) -CO-OH,

(6) -C≡N,

(7) $-CO-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) -C_1-C_6 alkyl unsubstituted or substituted with 1, 2, or 3 –F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0\text{-}2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) -SO_2-$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) -SO_2-(C_3-C_{12} alkyl),

(17) -NH-CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(18) -NH-CO-N(C_1-C_3 alkyl)$_2$,

(19) -N-CS-N(C_1-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-R_{N-5} where R_{N-5} is as defined above,

(21) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(22) -R_{N-4} where R_{N-4} is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH, or

(28) -S-(C_1-C_6 alkyl),

(C) -R_{N-aryl}-R_{N-aryl} where -R_{N-aryl} is as defined above,

(D) -R_{N-aryl}-$R_{N-heteroaryl}$ where -R_{N-aryl} and -$R_{N-heteroaryl}$ are as defined above,

(E) -$R_{N-heteroaryl}$-R_{N-aryl} where -R_{N-aryl} and -$R_{N-heteroaryl}$ are as defined above,

(F) -$R_{N-heteroaryl}$-$R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above,

(G) -R_{N-aryl}-O-R_{N-aryl} where -R_{N-aryl} is as defined above,

(H) -R_{N-aryl}-S-R_{N-aryl} where -R_{N-aryl} is as defined above,

(I) -$R_{N-heteroaryl}$-O-$R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above,

(J) -$R_{N-heteroaryl}$-S-$R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above,

(K) -R_{N-aryl}-CO-R_{N-aryl} where -R_{N-aryl} is as defined above,

(L) -R_{N-aryl}-CO-$R_{N-heteroaryl}$ where -R_{N-aryl} and $R_{N-heteroaryl}$ are as defined above,

(M) -R_{N-aryl}-SO_2-R_{N-aryl} where -R_{N-aryl} is as defined above,

(N) -$R_{N-heteroaryl}$-CO-$R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above,

(O) -$R_{N-heteroaryl}$-SO_2-$R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above,

(P) –R_{N-aryl}-O-(C_1-C_8 alkyl)-ϕ where R_{N-aryl} is as defined above,

(Q) –R_{N-aryl}-S-(C_1-C_8 alkyl)-ϕ where R_{N-aryl} is as defined above,

(R) $-R_{N\text{-heteroaryl}}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above, or

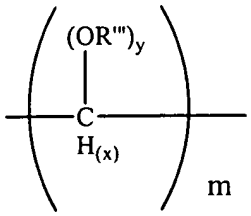
(S) $-R_{N\text{-heteroaryl}}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above,

(II) A-X_N- where X_N is –CO-,

wherein A is

(A) -T-E-$(Q)_{m'}$,

(1) where -T is



where

(a) x =1 when y = 1 and x = 2 when y = 0,

(b) m is 0, 1, 2 or 3,

(c) the values of x and y vary independently on each carbon when m is 2 and 3, and

(d) R'" varies independently on each carbon and is H, (C_1-C_2) alkyl, phenyl, or phenyl(C_1-C_3)alkyl;

(2) -E is

(a) C_1-C_5 alkyl, but only if m' does not equal 0,

(b) methylthioxy(C_2-C_4)alkyl,

(c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,

(f) biphenyl,

(g) diphenyl ether,

(h) diphenylketone,

(i) phenyl(C_1-C_8)alkyloxyphenyl, or

(j) C_1-C_6 alkoxy;

(3) -Q is

(a) C_1-C_3 alkyl,

(b) C_1-C_3 alkoxy,

(c) C_1-C_3 alkylthioxy,

(d) C_1-C_6 alkylacylamino,

(e) C_1-C_6 alkylacyloxy,

(f) amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary amino moieties),

(g) C_1-C_6 alkylamino

(h) phenylamino,

(i) carbamyl (including C_1-C_6 alkyl and phenyl amides and esters),

(j) carboxyl (including C_1-C_6 alkyl and phenyl esters),

(k) carboxy(C_2-C_5)alkoxy,

(l) carboxy(C_2-C5)alkylthioxy,

(m) heterocyclylacyl,

(n) heteroarylacyl, or

(o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) $-E(Q)_{m''}$ wherein E and -Q are as defined as above and m'' is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

(III) –CO-(C_1-C_6 alkyl) where alkyl is unsubstituted or substituted with one or two:

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} is the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(IV) –CO-(C_1-C_3 alkyl)-O-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(V) –CO-(C_1-C_3 alkyl)-S-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(VI) –CO-CH(-$(CH_2)_{0-2}$-O-R_{N-10})-$(CH_2)_{0-2}$-R_{N-aryl}/$R_{N-heteroaryl}$) where R_{N-aryl} and $R_{N-heteroaryl}$ are as defined above, where R_{N-10} is:

(A) –H,

(B) C_1-C_6 alkyl,

(C) C_3-C_7 cycloalkyl,

(D) C_2-C_6 alkenyl with one double bond,

(E) C_2-C_6 alkynyl with one triple bond,

(F) R_{1-aryl} where R_{1-aryl} is as defined above, or

(G) $R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above;

where B is -O-, -NH-, or -N(C_1-C_6 alkyl)-;

where R_C is:

(I) -(C_1-C_{10})alkyl-K_{1-3} in which:

(A) the alkyl chain is unsubstituted or substituted with one –OH,

(B) the alkyl chain is unsubstituted or substituted with one C_1-C_6 alkoxy unsubstituted or substituted with 1-5 -F,

(C) the alkyl chain is unsubstituted or substituted with one –O-ϕ,

(D) the alkyl chain is unsubstituted or substituted with 1-5 –F,

(E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

(1) H,

(2) C_1-C_3 alkyl,

(3) C_1-C_3 alkoxy,

(4) C_1-C_3 alkylthioxy,

(5) C_1-C_6 alkylacylamino,

(6) C_1-C_6 alkylacyloxy,

(7) amido

(8) C_1-C_6 alkylamino

(9) phenylamino,

(10) carbamyl

(11) carboxyl

(12) carboxy(C_2-C_5)alkoxy,

(13) carboxy(C_2-C5)alkylthioxy,

(14) heterocyclylacyl,

(15) heteroarylacyl,

(16) amino unsubstituted or substituted with C_1-C_6 alkyl,

(17) hydroxyl, or

(18) carboxyl methyl ester;

(II)-$(CH_2)_{0-3}$-J-[(-$(CH_2)_{0-3}$-K]$_{1-3}$ where K is as defined above and J is:

(A) a 5 to 7 atom monocyclic aryl group,

(B) a 8 to 12 atom multicyclic aryl group,

(C) a 5 to 7 atom heterocyclic group,

(D) a 8 to 12 atom multicyclic heterocyclic group, or

(E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -$(CH_2)_{0-3}$-(C_3-C_7) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

(A) C_1-C_3 alkyl unsubstituted or substituted with 1, 2, 3, or 4 –F, -Cl, -Br, or -I,

(B) -CO-OH,

(C) -CO-O-(C_1-C_4 alkyl),

(D) -OH, or

(E) C_1-C_6 alkoxy,

(IV) -$(CH_2)_{2-6}$-OH,

(V) -$(CR_{C-x}R_{C-y})_{0-4}$-R_{C-aryl} where R_{C-x} and R_{C-y} are –H, C_1-C_4 alkyl and ϕ- and R_{C-aryl} is the same as R_{N-aryl},

(VI) -$(CH_2)_{0-4}$-$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) isoxazolyl,

(Q) pyrazolyl,

(R) indolizinyl,

(S) indazolyl,

(T) benzothiazolyl,

(U) benzimidazolyl,

(V) benzofuranyl,

(W) furanyl,

(X) thienyl,

(Y) pyrrolyl,

(Z) oxadiazolyl,

(AA) thiadiazolyl,

(BB) triazolyl,

(CC) tetrazolyl,

(DD) 1, 4-benzodioxan

(EE) purinyl,

(FF) oxazolopyridinyl,

(GG) imidazopyridinyl,

(HH) isothiazolyl,

(II) naphthyridinyl,

(JJ) cinnolinyl,

(KK) carbazolyl,

(LL) β-carbolinyl,

(MM) isochromanyl,

(NN) chromanyl,

(OO) furazanyl,

(PP) tetrahydroisoquinoline,

(QQ) isoindolinyl,

(RR) isobenzotetrahydrofuranyl,

(SS) isobenzotetrahydrothienyl,

(TT) isobenzothiophenyl,

(UU) benzoxazolyl, or

(VV) pyridopyridinyl,

(VII) $-(CH_2)_{0-4}-R_{C\text{-}heterocycle}$ where $R_{C\text{-}heterocycle}$ is the same as $R_{1\text{-}heterocycle}$,

(VIII) $-C(R_{C\text{-}1})(R_{C\text{-}2})-CO-NH-R_{C\text{-}3}$ where $R_{C\text{-}1}$ and $R_{C\text{-}2}$ are the same or different and are:

(A) -H,

(B) $-C_1-C_6$ alkyl,

(C) $-(C_1-C_4$ alkyl$)-R_{C'\text{-}aryl}$ where $R_{C'\text{-}aryl}$ is as defined above for $R_{1\text{-}aryl}$,

(D) $-(C_1-C_4$ alkyl$)-R_{C\text{-}heteroaryl}$ where $R_{C\text{-}heteroaryl}$ is as defined above,

(E) $-(C_1-C_4$ alkyl$)-R_{C\text{-}heterocycle}$ where $R_{C\text{-}heterocycle}$ is as defined above,

(F) $-R_{C\text{-}heteroaryl}$ where $R_{C\text{-}heteroaryl}$ is as defined above,

(G) $-R_{C\text{-}heterocycle}$ where $R_{C\text{-}heterocycle}$ is as defined above,

(H) $-(CH_2)_{1-4}-OH$,

(I) $-(CH_2)_{1-4}-R_{C\text{-}4}-(CH_2)_{1-4}-R_{C'\text{-}aryl}$ where $R_{C\text{-}4}$ is –O-, -S-, -NH- or

$-NHR_{C\text{-}5}$- where $R_{C\text{-}5}$ is C_1-C_6 alkyl, and where $R_{C'\text{-}aryl}$ is as defined above,

(J) $-(CH_2)_{1\text{-}4}$-$R_{C\text{-}4}$-$(CH_2)_{1\text{-}4}$-$R_{C\text{-}heteroaryl}$ where $R_{C\text{-}4}$ and $R_{C\text{-}heteroaryl}$ are as defined above, or

(K) $-R_{C'\text{-}aryl}$ where $R_{C'\text{-}aryl}$ is as defined above,

and where $R_{C\text{-}3}$ is:

(A) -H,

(B) -C_1-C_6 alkyl,

(C) $-R_{C'\text{-}aryl}$ where $R_{C'\text{-}aryl}$ is as defined above,

(D) $-R_{C\text{-}heteroaryl}$ where $R_{C\text{-}heteroaryl}$ is as defined above,

(E) $-R_{C\text{-}heterocycle}$ where $R_{C\text{-}heterocycle}$ is as defined above,

(F) -(C_1-C_4 alkyl)-$R_{C'\text{-}aryl}$ where $R_{C'\text{-}aryl}$ is as defined above,

(G) -(C_1-C_4 alkyl)-$R_{C\text{-}heteroaryl}$ where $R_{C\text{-}heteroaryl}$ is as defined above, or

(H) -(C_1-C_4 alkyl)-$R_{C\text{-}heterocycle}$ where $R_{C\text{-}heterocycle}$ is as defined above,

(IX) $-CH(\phi)_2$,

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

(A) C_1-C_3 alkyl,

(B) $-CF_3$,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) $-OCF_3$,

(F) $-NH_2$,

(G) -OH, or

(H) -C≡N,

(XI) $-CH_2$-C≡CH;

(XII) $-(CH_2)_{0\text{-}1}$-$CHR_{C\text{-}5}$-$(CH_2)_{0\text{-}1}$-ϕ where $R_{C\text{-}5}$ is:

(A) –OH, or

(B)-CH_2-OH;

(XIII) –CH(-ϕ)-CO-O(C_1-C_3 alkyl);

(XIV) –CH(-CH_2-OH)-CH(-OH)-ϕ-NO_2;

(XV) –$(CH_2)_2$-O-$(CH_2)_2$-OH;

(XVI) –CH_2-NH-CH_2-CH(-O-CH_2-$CH_3)_2$;

(XVII) -(C_2-C_8) alkynyl; or

(XVIII) –H; or a pharmaceutically acceptable salt thereof.

2. A method for inhibiting β-secretase activity according to 1

where R_1 is:

(V) -$(CH_2)_{0-3}$-($R_{1\text{-aryl}}$), or

(VI) -$(CH_2)_{n1}$-($R_{1\text{-heteroaryl}}$)

where R_N is:

(I) R_{N-1}-X_N- where X_N is:

(A) –CO-, or

(B) –SO_2-,

where R_{N-1} is:

(A) $R_{N\text{-aryl}}$, or

(B) -$R_{N\text{-heteroaryl}}$,

(VI) –CO-CH(-$(CH_2)_{0-2}$-O-R_{N-10})-$(CH_2)_{0-2}$-$R_{N\text{-aryl}}$/$R_{N\text{-heteroaryl}}$)

where R_C is:

(I)-C_1-C_8 alkyl,

(III) -$(CH_2)_{0-3}$-(C_3-C_7) cycloalkyl,

(IV) -$(CH_2)_{0-3}$-OH,

(V) -$(CR_{C-x}R_{C-y})_{0-4}$-$R_{C\text{-aryl}}$,

(VI) -$(CH_2)_{0-4}$-$R_{C\text{-heteroaryl}}$,

(VII) -$(CH_2)_{0-4}$-$R_{C\text{-heterocycle}}$,

(VIII) -C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3}, or

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one or two:

(A) C_1-C_3 alkyl,

(B) $-CF_3$,

(C) -F, Cl, -Br or –I,

(D) C_1-C_3 alkoxy, or

(E) $-OCF_3$.

3. A method for inhibiting β-secretase activity according to claim 85 where R_1 is:

(V) $-CH_2-(R_{1\text{-aryl}})$, or

(VI) $-CH_2-(R_{1\text{-heteroaryl}})$;

where R_2 is –H;

where R_N is:

(I) $R_{N\text{-}1}$-X_N- where X_N is:

(A) –CO-,

where $R_{N\text{-}1}$ is:

(A) $R_{N\text{-aryl}}$, or

(B) $-R_{N\text{-heteroaryl}}$,

where R_C is:

(III) $-(CH_2)_{0\text{-}3}-(C_3\text{-}C_7)$ cycloalkyl,

(V) $-(CR_{C\text{-}x}R_{C\text{-}y})_{0\text{-}4}-R_{C\text{-aryl}}$,

(VI) $-(CH_2)_{0\text{-}4}-R_{C\text{-heteroaryl}}$,

(VII) $-(CH_2)_{0\text{-}4}-R_{C\text{-heterocycle}}$,

(VIII) $-C(R_{C\text{-}1})(R_{C\text{-}2})$-CO-NH-$R_{C\text{-}3}$, or

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring.

4. A method for inhibiting β-secretase activity according to claim 3 where R_C is:

(V) $-(CR_{C\text{-}x}R_{C\text{-}y})_{0\text{-}4}-R_{C\text{-aryl}}$,

(VI) $-(CH_2)_{0\text{-}4}-R_{C\text{-heteroaryl}}$, or

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring.

5. A method for inhibiting β-secretase activity according to claim 1 where R_1 is:

$-CH_2-(R_{1\text{-aryl}})$ where $R_{1\text{-aryl}}$ is phenyl.

6. A method for inhibiting β-secretase activity according to claim 5 where R_1 is:

$-CH_2-(R_{1\text{-aryl}})$ where $R_{1\text{-aryl}}$ is phenyl substituted with two –F.

7. A method for inhibiting β-secretase activity according to claim 6 where phenyl is substituted with two –F in the 3- and 5- positions giving 3,5-difluorophenyl.

8. A method for inhibiting β-secretase activity according to claim 1 where R_2 is:

(I) –H,

(II) C_1-C_6 alkyl, or

(III) $-(CH_2)_{0\text{-}4}-R_{2\text{-}1}$ where $R_{2\text{-}1}$ is $R_{1\text{-aryl}}$.

9. A method for inhibiting β-secretase activity according to claim 1 where R_2 is:

(II) C_1-C_6 alkyl, or

(III) benzyl.

10. A method for inhibiting β-secretase activity according to claim 1 where R_N is $R_{N\text{-}1}$-X_N- where X_N is –CO-, where $R_{N\text{-}1}$ is $R_{N\text{-aryl}}$ where $R_{N\text{-aryl}}$ is phenyl substituted with one $-CO-NR_{N\text{-}2}R_{N\text{-}3}$ where the substitution on phenyl is 1,3-.

11. A method for inhibiting β-secretase activity according to claim 1 where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are the same and are C_3 alkyl.

12. A method for inhibiting β-secretase activity according to claim 1 where R_N is $R_{N\text{-}1}$-X_N- where X_N is–CO-, where $R_{N\text{-}1}$ is $R_{N\text{-aryl}}$ where $R_{N\text{-aryl}}$ is phenyl substituted with one C_1 alkyl and with one $-CO-NR_{N\text{-}2}R_{N\text{-}3}$ where the substitution on the phenyl is 1,3,5-.

13. A method for inhibiting β-secretase activity according to claim 12 where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are the same and are C_3 alkyl.

14. A method for inhibiting β-secretase activity according to claim 1 where R_N is

R_{N-1}-X_N- where X_N is –CO-, where R_{N-1} is $R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is substituted with one -CO-$NR_{N-2}R_{N-3}$.

15. A method for inhibiting β-secretase activity according to claim 1 where R_{N-2} and R_{N-3} are the same and are -C_3 alkyl.

16. A method for inhibiting β-secretase activity according to claim 1 where R_N is:

A-X_N- where X_N is –CO-, where A is:

(C) $C_{10}H_7$-CH(OH)-, or

(D) t-butoxy.

17. A method for inhibiting β-secretase activity according to claim 1 where R_C is:

(V) -$(CR_{C-x}R_{C-y})_{0-4}$-$R_{C\text{-aryl}}$,

(VI) -$(CH_2)_{0-4}$-$R_{C\text{-heteroaryl}}$,

(VII) -$(CH_2)_{0-4}$-$R_{C\text{-heterocycle}}$,

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one or two:

(A) C_1-C_3 alkyl,

(B) –CF_3,

(C) -F, Cl, -Br or –I,

(D) C_1-C_3 alkoxy,

(E) -OCF_3, or

(XVIII) –H.

18. A method for inhibiting β-secretase activity according to claim 17 where R_C is:

(V) -$(CR_{C-x}R_{C-y})_{0-4}$-$R_{C\text{-aryl}}$ where $R_{C\text{-aryl}}$ is phenyl.

19. A method for inhibiting β-secretase activity according to claim 18 where phenyl substituted in the 3-position or 3,5-positions.

20. A method for inhibiting β-secretase activity according to claim 17 where R_C is:

(VI) -CH_2-$R_{C\text{-}heteroaryl}$,

21. A method for inhibiting β-secretase activity according to claim 17 where R_C is:

(VII) -CH_2-$R_{C\text{-}heterocycle}$.

22. A method for inhibiting β-secretase activity according to claim 17 where R_C is:

(X) -cyclohexyl ring fused to a phenyl ring.

23. A method for inhibiting β-secretase activity according to claim 1 where R_C is:

(I) -(C_1-C_{10})alkyl-$K_{1\text{-}3}$ where each K is:

(1) H,

(11) carboxyl,

(16) amino unsubstituted or substituted with C_1-C_6 alkyl; or

(18) carboxyl methyl ester;

(II) -$(CH_2)_{0\text{-}3}$-J-[-K]$_{1\text{-}3}$, where J is:

(A) a 5 to 7 atom monocyclic aryl group, or

(B) a 5 to 10 atom multicyclic cycloalkyl group,

and each K is:

(1) H,

(3) C_1-C_3 alkoxy, or

(11) carboxyl,

(III) -$(CH_2)_{0\text{-}3}$-(C_3-C_7) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three:

(B) -CO-OH,

(C) -CO-O-(C_1-C_4 alkyl), or

(E) C_1-C_6 alkoxy,

(IV) -$(CH_2)_{2\text{-}6}$-OH,

(V) -$(CH_2)_{0\text{-}4}$-$R_{C\text{-}aryl}$,

(VI) -$(CH_2)_{0\text{-}4}$-$R_{C\text{-}heteroaryl}$,

(VII) -$(CH_2)_{0\text{-}4}$-$R_{C\text{-}heterocycle}$, or

(XVIII) -(C_2-C_8) alkynyl.

24. A method for inhibiting β-secretase activity according to claim 1 where R_C is:

(I) -(C_1-C_{10})alkyl-K where K is H, carboxyl, carboxyl methyl ester, amino unsubstituted or substituted with C_1-C_6 alkyl,

(II) a benzyl or phenylpropyl group substituted with a carboxyl group,

(III) -$(CH_2)_{0-3}$-(C_3-C_7) cycloalkyl where cycloalkyl is cyclohexyl, cyclohexyl substituted with 1 or 2 carboxyl groups, or cyclohexyl substituted with 1 or 2 alkoxy groups,

(V) -$(CH_2)_{0-4}$-phenyl substituted or unsubstituted with F,

(VI) -$(CH_2)_{0-4}$-heteroaryl, or

(VII) selected from -$(CH_2)_{0-4}$-morpholinyl and -$(CH_2)_{0-4}$-tetrahydrofuryl.

25. A method for inhibiting β-secretase activity according to claim 1 where R_C is:

(I) C_5H_{10}-K or C_7H_{14}-K where K is carboxyl or carboxyl methyl ester,

(II) a benzyl or phenylpropyl group substituted with a carboxyl group at the 5-position, or

(III) a cyclohexyl ring substituted at the 3- and 5- positions or at the 4-position with a carboxyl group.

26. A method for inhibiting β-secretase activity according to claim 1

where R_1 is:

(I) C_1-C_5 alkyl,

(II) –$(CH_2)_{1-2}$-S-CH_3,

(IV) C_1-C_5 alkenyl,

(V) -$(CH_2)_{0-3}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above, and

(VI) -$(CH_2)_{0-3}$-($R_{1\text{-heteroaryl}}$) where $R_{1\text{-heteroaryl}}$ is as defined above,

wherein any of the above are unsubstituted or substituted with up to two C_1-C_3 alkyl, –F, -Cl, -Br, -I, or -CF_3;

where R_2 is:

(I) -H,

(II) C_1-C_6 alkyl, or

(III) $-(CH_2)_{0-3}-R_{2-1}$ where R_{2-1} is (C_3-C_6)cycloalkyl, $R_{1\text{-aryl}}$ or $R_{1\text{-heteroaryl}}$ where R_1-aryl is a 5 or 6-membered aryl group and $R_{1\text{-heteroaryl}}$ is as defined above;

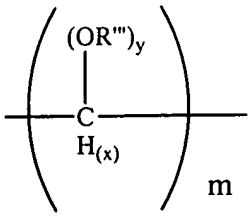
where R_N is:

(II) $A-X_N-$ where X_N is –CO-,

wherein A is

(A) -T-E-$(Q)_{m'}$,

(1) where -T is



where

(a) x =1 when y = 1 and x = 2 when y = 0,

(b) m is 0, 1, 2 or 3,

(c) the values of x and y vary independently on each carbon when m is 2 and 3, and

(d) R'" varies independently on each carbon and is H, (C_1-C_2) alkyl, phenyl, or phenyl(C_1-C_3)alkyl;

(2) -E is

(a) C_1-C_5 alkyl, but only if m' does not equal 0,

(b) methylthioxy(C_2-C_4)alkyl,

(c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,

(f) biphenyl,

(g) diphenyl ether,

(h) diphenylketone,

(i) phenyl(C_1-C_8)alkyloxyphenyl, or

(j) C_1-C_6 alkoxy;

(3) -Q is

(a) C_1-C_3 alkyl,

(b) C_1-C_3 alkoxy,

(c) C_1-C_3 alkylthioxy,

(d) C_1-C_6 alkylacylamino,

(e) C_1-C_6 alkylacyloxy,

(f) amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary amino moieties),

(g) C_1-C_6 alkylamino

(h) phenylamino,

(i) carbamyl (including C_1-C_6 alkyl and phenyl amides and esters),

(j) carboxyl (including C_1-C_6 alkyl and phenyl esters),

(k) carboxy(C_2-C_5)alkoxy,

(l) carboxy(C_2-C5)alkylthioxy,

(m) heterocyclylacyl,

(n) heteroarylacyl, or

(o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) $-E(Q)_{m''}$ wherein E and -Q are as defined as above and m" is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

where R_C is:

(I) -(C_1-C_{10})alkyl-$K_{1\text{-}3}$

(E) the alkyl chain optionally contains a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

(2) C_1-C_3 alkyl,

(3) C_1-C_3 alkoxy,

(4) C_1-C_3 alkylthioxy,

(5) C_1-C_6 alkylacylamino,

(6) C_1-C_6 alkylacyloxy,

(7) amido,

(8) C_1-C_6 alkylamino

(9) phenylamino,

(10) carbamyl,

(11) carboxyl,

(12) carboxy(C_2-C_5)alkoxy,

(13) carboxy(C_2-C5)alkylthioxy,

(14) heterocyclylacyl,

(15) heteroarylacyl,

(16) amino unsubstituted or substituted with C_1-C_6 alkyl,

(17) hydroxyl, or

(18) carboxyl methyl ester;

(II) $-(CH_2)_{0-3}$-J-$[(-(CH_2)_{0-3}$-K$]_{1-3}$ where K is:

(2) C_1-C_3 alkyl,

(3) C_1-C_3 alkoxy,

(4) C_1-C_3 alkylthioxy,

(5) C_1-C_6 alkylacylamino,

(6) C_1-C_6 alkylacyloxy,

(7) amido,

(8) C_1-C_6 alkylamino

(9) phenylamino,

(10) carbamyl,

(11) carboxyl,

(12) carboxy(C_2-C_5)alkoxy,

(13) carboxy(C_2-C5)alkylthioxy,

(14) heterocyclylacyl,

(15) heteroarylacyl,

(16) amino unsubstituted or substituted with C_1-C_6 alkyl,

(17) hydroxyl, or

(18) carboxyl methyl ester;

J is:

(A) a 5 to 7 atom monocyclic aryl group,

(B) a 8 to 12 atom multicyclic aryl group,

(C) a 5 to 7 atom monocyclic heterocyclic group,

(D) a 8 to 12 atom multicyclic heterocyclic group, or

(E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

and

where B is O or NH.

27. A method for inhibiting β-secretase activity according to claim 1 where the pharmaceutically acceptable salt is a salt of hydrochloric, hydrobromic, hydroiodic, nitric, sulfuric, phosphoric, citric, methanesulfonic, CH_3-$(CH_2)_n$-COOH where n is 0 thru 4, HOOC-(CH_2)n-COOH where n is as defined above, HOOC-CH=CH-COOH and ϕ-COOH acid or triethanolamine, N-methylglucamine, diethanolamine, ethanolamine, tris(hydroxymethyl)aminomethane (TRIS), ammonia, or carbonate, bicarbonate, phosphonate, or hydroxide salts of an alkali or alkaline earth metal.

28. A method for inhibiting β-secretase activity according to claim 1 wherein said compound is:

N-[(1*S*, 2*S*, 4*R*)-1-(3,5-Difluorobenzyl)-4-(*syn*, *syn*)-(3,5-dimethoxycyclohexylcarbamoyl)-2-hydroxyhexyl]-*N,N*-dipropylisophathalamide,

6-[6-(3,5-Difluorophenyl)-5-(*S*)-(3-dipropylcarbamoylbenzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxyhexanoylamino]-hexanoic acid,

5-[6-(3,5-Difluorophenyl)-5-(*S*)-(3-dipropylcarbamoylbenzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxyhexanoylamino]-pentanoic acid,

4-[6-(3,5-Difluorophenyl)-5-(*S*)-(3-dipropylcarbamoylbenzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxyhexanoylamino]-butyric acid,

3-[6-(3,5-Difluorophenyl)-5-(*S*)-(3-dipropylcarbamoylbenzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxyhexanoylamino]-propionic acid,

8-[6-(3,5-Difluorophenyl)-5-(*S*)-(3-dipropylcarbamoylbenzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxyhexanoylamino]-octanoic acid,

8-[6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-octanoic acid methyl ester,

N-[4-(*R*)-Butylcarbamoyl-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,

N-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(R)-isobutylcarbamoyl-hexyl]-*N,N*-dipropyl-isophthalamide,

N-[4-(*R*)-Benzylcarbamoyl-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,

N-[4-(*R*)-(Cyclohexylmethyl-carbamoyl)-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,

N-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-(piperidine-1-carbonyl)-hexyl]-*N,N*-dipropyl-isophthalamide,

N-[1-(*S*)-(3,5-Difluoro-benzyl)-4-(*R*)-(2-dimethylamino-ethylcarbamoyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,

N-[4-(*R*)-(Butyl-methyl-carbamoyl)-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,

N-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-(3-hydroxy-propylcarbamoyl)-hexyl]-*N,N*-dipropyl-isophthalamide,

4-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid methyl ester,

N-[1-(*S*)-(3,5-Difluoro-benzyl)-4-(*R*)-(3-dimethylamino-propylcarbamoyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-2-(*R*)-methyl-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-2-(*R*)-propyl-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxyl-2-(*R*)-isobutyl-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,

4-(*anti*)-([2-(*R*)-Benzyl-6-(3,5-difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-5-methyl-benzoylamino)-2-(*R*)-ethyl-4-(S)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-5-methyl-benzoylamino)-2-(*R*)-ethyl-4-(S)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid methyl ester,

N-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-(2-morpholin-4-yl-ethylcarbamoyl)-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,

N-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-isobutylcarbamoyl-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,

N-[4-(*R*)-(2-Diethylamino-ethylcarbamoyl)-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,

N-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-[(tetrahydro-furan-2-ylmethyl)-carbamoyl]-pentyl)-5-methyl-*N,N*-dipropyl-isophthalamide,

N-[4-(*R*)-(Adamantan-2-ylcarbamoyl)-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,

N-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-methyl-5-morpholin-4-yl-5-oxo-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,

N-[4-(*R*)-Benzylcarbamoyl-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,

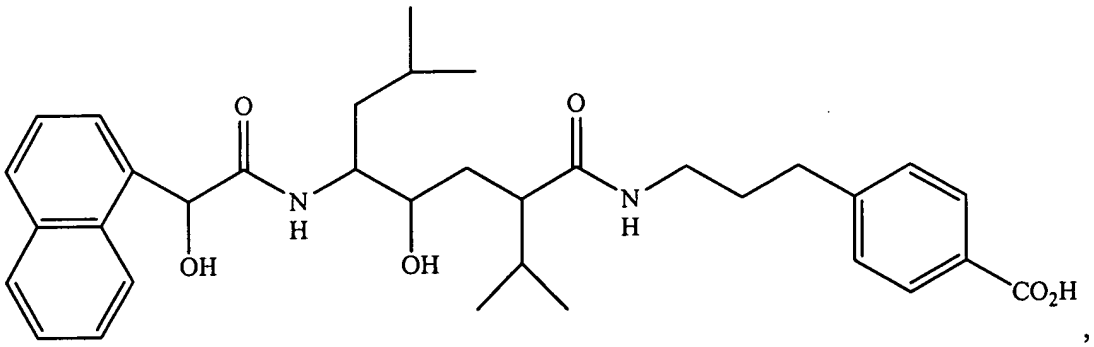
N-[1-(*S*)-(3,5-Difluoro-benzyl)-4-(*R*)-(4-fluoro-benzylcarbamoyl)-2-(*S*)-hydroxy-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,

N-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-phenethylcarbamoyl-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,

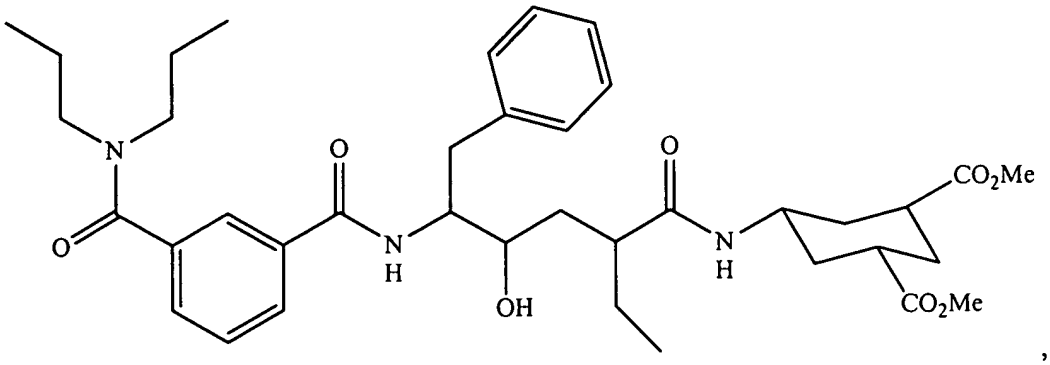
N-[1-(*S*)-(3,5-Difluoro-benzyl)-4-(*R*)-[(furan-2-ylmethyl)-carbamoyl]-2-(S)-hydroxy-pentyl)-5-methyl-*N,N*-dipropyl-isophthalamide, or

N-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-(prop-2-ynylcarbamoyl)-pentyl]-5-methy-*N,N*-dipropyl-isophthalamide.

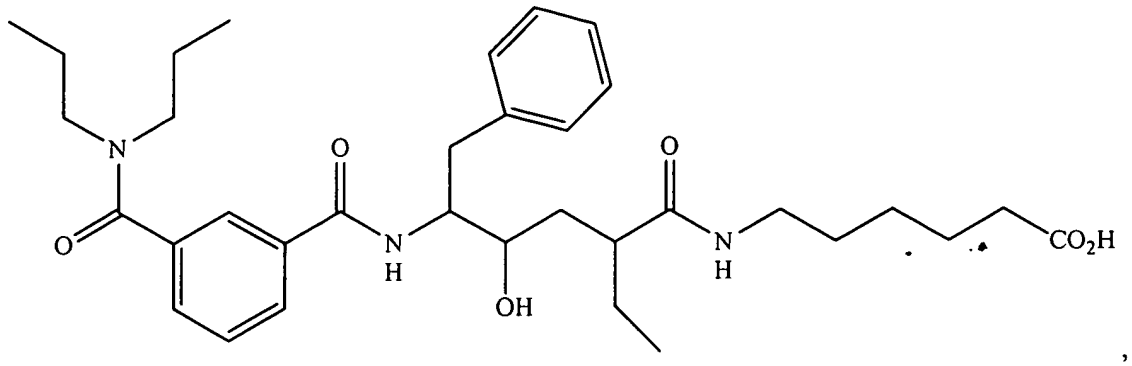
29. A method for inhibiting β-secretase activity according to claim 1 wherein said compound is:

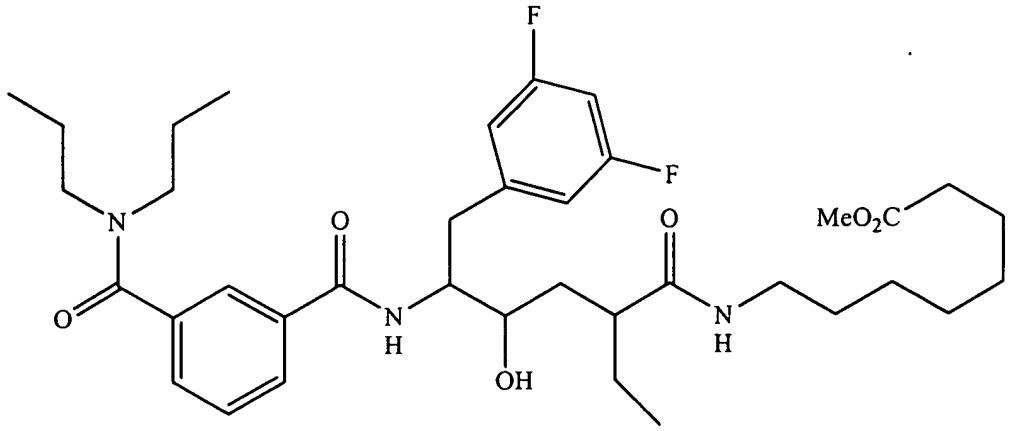


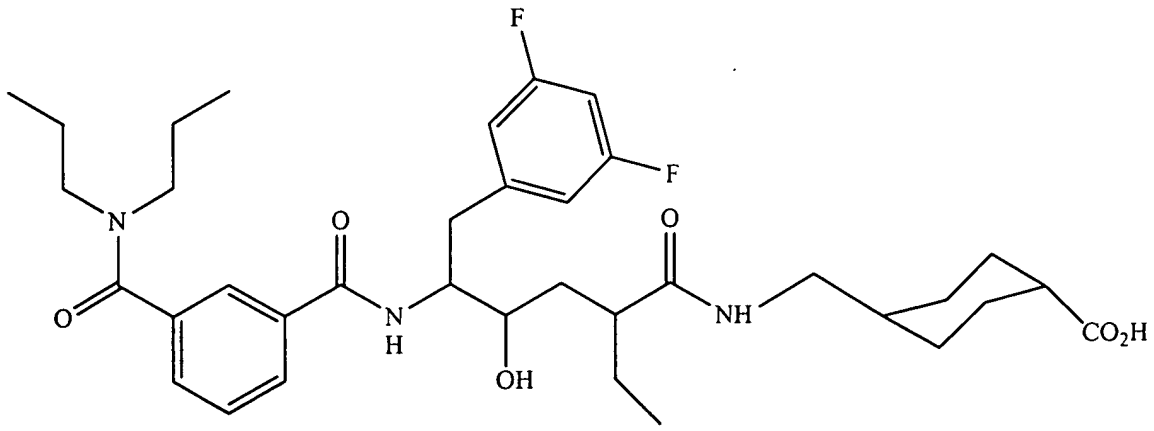
,

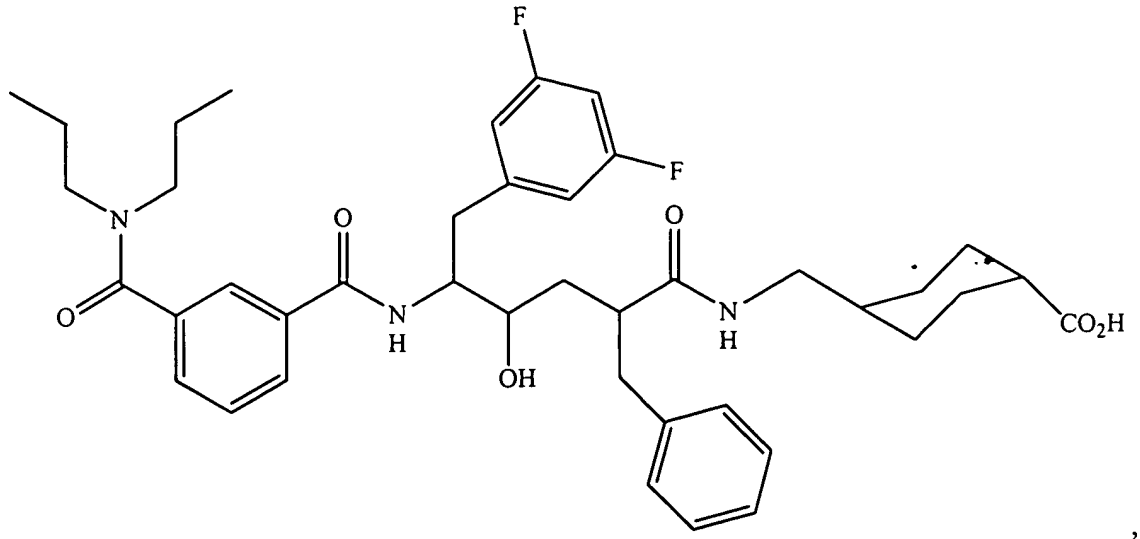


,

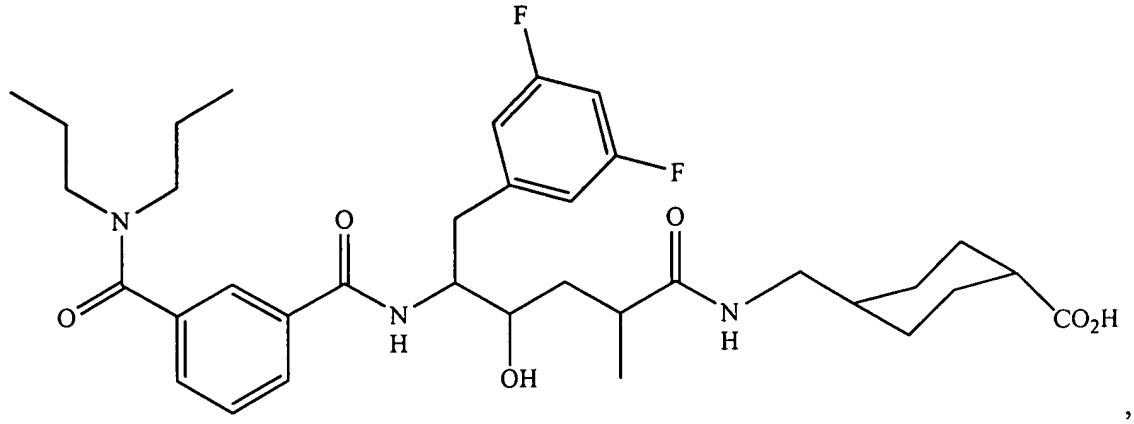






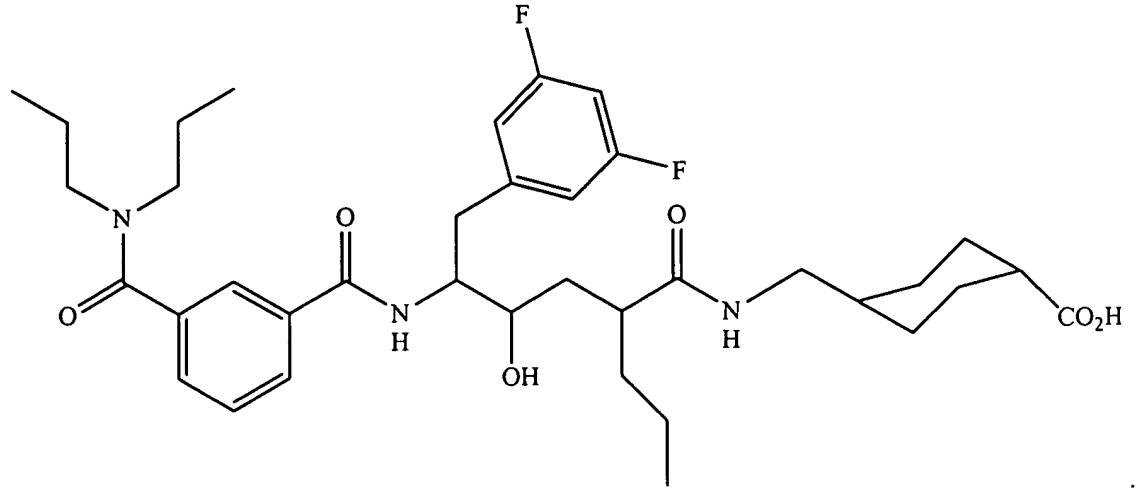


,



,

or



.

30. The method of claim 1, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 0.1nM to about 200μM.

31. The method of claim 30, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 10nM to about 100μM.

32. The method of claim 31, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 100nM to about 50μM.

33. The method of claim 32, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 1μM to about 10μM.

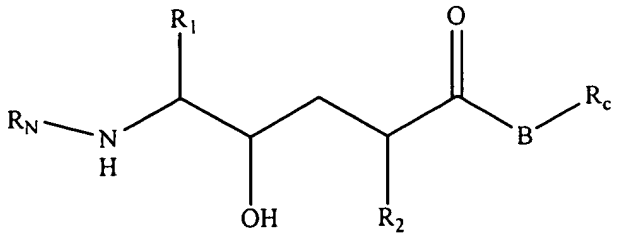
34. The method of claim 1, wherein said β-secretase is exposed to said compound *in vitro*.

35. The method of claim 1, wherein said β-secretase is exposed to said compound in a cell.

36. The method of claim 35, wherein said cell is in an animal.

37. The method of claim 36, wherein said animal is a human.

38. A method for inhibiting amyloid precursor protein (APP) cleavage in a reaction mixture at a site between Met596 and Asp597, numbered for the APP-695 amino acid isotype; or at a corresponding site of an isotype or mutant thereof, comprising exposing said reaction mixture to an effective inhibitory amount of a hydroxyethylene compound of the formula



(XII)

where R_1 is:

(I) C_1-C_6 alkyl, unsubstituted or substituted with one, two or three C_1-C_3 alkyl, –F, -Cl, -Br, -I, -OH, $-NH_2$, -C≡N, $-CF_3$, or $-N_3$,

(II) $-(CH_2)_{1-2}$-S-CH_3,

(III) $-CH_2$-CH_2-S-CH_3,

(IV) $-CH_2$-(C_2-C_6 alkenyl) unsubstituted or substituted by one –F,

(V) $-(CH_2)_{0-3}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:

(A) C_1-C_3 alkyl,

(B) $-CF_3$,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) –O-CF_3,

(F) $-NH_2$,

(G) -OH, or

(H) -C≡N,

(VI) $-(CH_2)_{n1}$-($R_{1\text{-heteroaryl}}$) where n_1 is 0, 1, 2, or 3 and $R_{1\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{1\text{-heteroaryl}}$ group is bonded to $-(CH_2)_{0\text{-}3}-$ by any ring atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_3 alkyl,

(2) $-CF_3$,

(3) -F, Cl, -Br, or –I,

(4) C_1-C_3 alkoxy,

(5) $-O-CF_3$,

(6) $-NH_2$,

(7) -OH, or

(8) $-C\equiv N$,

with the proviso that when n_1 is zero $R_{1\text{-heteroaryl}}$ is not bonded to the carbon chain by nitrogen, or

(VII) $-(CH_2)_{n1}-(R_{1\text{-heterocycle}})$ where n_1 is as defined above and

$R_{1\text{-heterocycle}}$ is:

(A) morpholinyl,

(B) thiomorpholinyl,

(C) thiomorpholinyl S-oxide,

(D) thiomorpholinyl S,S-dioxide,

(E) piperazinyl,

(F) homopiperazinyl,

(G) pyrrolidinyl,

(H) pyrrolinyl,

(I) tetrahydropyranyl,

(J) piperidinyl,

(K) tetrahydrofuranyl, or

(L) tetrahydrothiophenyl,

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

(1) =O,

(2) C_1-C_3 alkyl,

(3) $-CF_3$,

(4) -F, Cl, -Br and –I,

(5) C_1-C_3 alkoxy,

(6) $-O-CF_3$,

(7) $-NH_2$,

(8) -OH, or

(9) -C≡N,

with the proviso that when n_1 is zero $R_{1\text{-heterocycle}}$ is not bonded to the carbon chain by nitrogen;

where R_2 is:

(I) -H,

(II) C_1-C_6 alkyl, or

(III) $-(CH_2)_{0\text{-}4}-R_{2\text{-}1}$ where $R_{2\text{-}1}$ is (C_3-C_6)cycloalkyl, $R_{1\text{-aryl}}$ or $R_{1\text{-heteroaryl}}$ where $R_{1\text{-aryl}}$ and $R_{1\text{-heteroaryl}}$ are as defined above,

where R_N is:

(I) R_{N-1}-X_N- where X_N is:

(A) –CO-,

(B) $–SO_2$-,

(C) -$(CR'R'')_{1-6}$ where R' and R" are the same or different and are –H or C_1-C_4 alkyl,

(D) –CO-$(CR'R'')_{1-6}$-X_{N-1} where X_{N-1} is –O-, -S- and –NR'R"- and where R' and R" are as defined above,

(E) a single bond;

where R_{N-1} is:

(A) $R_{N\text{-}aryl}$ where $R_{N\text{-}aryl}$ is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or -I,

(3) -OH,

(4) $-NO_2$,

(5) -CO-OH,

(6) -C≡N,

(7) -CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) -C_1-C_6 alkyl unsubstituted or substituted with one to three –F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e) -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0\text{-}2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) -SO_2-$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) -SO_2-(C_3-C_{12} alkyl),

(17) -NH-CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(18) -NH-CO-N(C_1-C_3 alkyl)$_2$,

(19) -N-CS-N(C_1-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(21) -$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ can be the same or different and are as defined above,

(22) -$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH,

(28) -S-(C_1-C_6 alkyl),

(29) C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F,

(30) –O-(C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F, or

(31) –O-ϕ,

(B) -$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{N\text{-heteroaryl}}$ group is bonded by any atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{N\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or - I,

(3) -OH,

(4) $-NO_2$,

(5) -CO-OH,

(6) -C≡N,

(7) $-CO-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) -C_1-C_6 alkyl unsubstituted or substituted with 1, 2, or 3 –F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) $-R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above,

or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0\text{-}2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) -SO_2-$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) -SO_2-(C_3-C_{12} alkyl),

(17) -NH-CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(18) -NH-CO-N(C_1-C_3 alkyl)$_2$,

(19) -N-CS-N(C_1-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(21) -$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ can be the same or different and are as defined above,

(22) -$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH, or

(28) -S-(C_1-C_6 alkyl),

(C) -$R_{N\text{-aryl}}$-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(D) -$R_{N\text{-aryl}}$-$R_{N\text{-heteroaryl}}$ where -$R_{N\text{-aryl}}$ and -$R_{N\text{-heteroaryl}}$ are as defined above,

(E) -$R_{N\text{-heteroaryl}}$-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ and -$R_{N\text{-heteroaryl}}$ are as defined above,

(F) -$R_{N\text{-heteroaryl}}$-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(G) -$R_{N\text{-aryl}}$-O-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(H) -$R_{N\text{-aryl}}$-S-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(I) -$R_{N\text{-heteroaryl}}$-O-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(J) -$R_{N\text{-heteroaryl}}$-S-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(K) -$R_{N\text{-aryl}}$-CO-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(L) -$R_{N\text{-aryl}}$-CO-$R_{N\text{-heteroaryl}}$ where -$R_{N\text{-aryl}}$ and $R_{N\text{-heteroaryl}}$ are as defined above,

(M) -$R_{N\text{-aryl}}$-SO_2-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(N) -$R_{N\text{-heteroaryl}}$-CO-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(O) -$R_{N\text{-heteroaryl}}$-SO_2-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(P) –$R_{N\text{-aryl}}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-aryl}}$ is as defined above,

(Q) –$R_{N\text{-aryl}}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-aryl}}$ is as defined above,

(R) –$R_{N\text{-heteroaryl}}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above, or

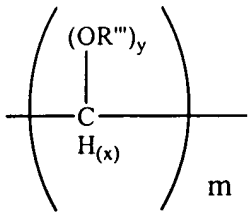
(S) –$R_{N\text{-heteroaryl}}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above,

(II) A-X_N- where X_N is –CO-,

wherein A is

(A) -T-E-$(Q)_{m'}$,

(1) where -T is



where

(a) x =1 when y = 1 and x = 2 when y = 0,

(b) m is 0, 1, 2 or 3,

(c) the values of x and y vary independently on each carbon when m is 2 and 3, and

(d) R'" varies independently on each carbon and is H, (C_1-C_2) alkyl, phenyl, or phenyl(C_1-C_3)alkyl;

(2) -E is

(a) C_1-C_5 alkyl, but only if m' does not equal 0,

(b) methylthioxy(C_2-C_4)alkyl,

(c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,

(f) biphenyl,

(g) diphenyl ether,

(h) diphenylketone,

(i) phenyl(C_1-C_8)alkyloxyphenyl, or

(j) C_1-C_6 alkoxy;

(3) -Q is

(a) C_1-C_3 alkyl,

(b) C_1-C_3 alkoxy,

(c) C_1-C_3 alkylthioxy,

(d) C_1-C_6 alkylacylamino,

(e) C_1-C_6 alkylacyloxy,

(f) amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary amino moieties),

(g) C_1-C_6 alkylamino

(h) phenylamino,

(i) carbamyl (including C_1-C_6 alkyl and phenyl amides and esters),

(j) carboxyl (including C_1-C_6 alkyl and phenyl esters),

(k) carboxy(C_2-C_5)alkoxy,

(l) carboxy(C_2-C5)alkylthioxy,

(m) heterocyclylacyl,

(n) heteroarylacyl, or

(o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) $-E(Q)_{m''}$ wherein E and -Q are as defined as above and m'' is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

(III) –CO-(C_1-C_6 alkyl) where alkyl is unsubstituted or substituted with one or two:

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) $-CO-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) $-CO-R_{N-4}$ where R_{N-4} is as defined above,

(G) $-SO_2-(C_1-C_8$ alkyl),

(H) $-SO_2-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) $-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) $-R_{N-4}$ where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) $-O-CO-NR_{N-8}R_{N-8}$ where the R_{N-8} is the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(IV) $-CO-(C_1-C_3$ alkyl)-O-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) $-CO-O-R_{N-8}$ where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) $-CO-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) $-CO-R_{N-4}$ where R_{N-4} is as defined above,

(G) $-SO_2-(C_1-C_8$ alkyl),

(H) $-SO_2-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) $-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(V) –CO-(C_1-C_3 alkyl)-S-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(VI) –CO-CH(-$(CH_2)_{0-2}$-O-R_{N-10})-$(CH_2)_{0-2}$-$R_{N\text{-}aryl}$/$R_{N\text{-}heteroaryl}$) where $R_{N\text{-}aryl}$ and $R_{N\text{-}heteroaryl}$ are as defined above, where R_{N-10} is:

(A) –H,

(B) C_1-C_6 alkyl,

(C) C_3-C_7 cycloalkyl,

(D) C_2-C_6 alkenyl with one double bond,

(E) C_2-C_6 alkynyl with one triple bond,

(F) $R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(G) $R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above;

where B is -O-, -NH-, or -N(C_1-C_6 alkyl)-;

where R_C is:

(I) -(C_1-C_{10})alkyl-$K_{1\text{-}3}$ in which:

(A) the alkyl chain is unsubstituted or substituted with one –OH,

(B) the alkyl chain is unsubstituted or substituted with one C_1-C_6 alkoxy unsubstituted or substituted with 1-5 -F,

(C) the alkyl chain is unsubstituted or substituted with one –O-ϕ,

(D) the alkyl chain is unsubstituted or substituted with 1-5 –F,

(E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

(1) H,

(2) C_1-C_3 alkyl,

(3) C_1-C_3 alkoxy,

(4) C_1-C_3 alkylthioxy,

(5) C_1-C_6 alkylacylamino,

(6) C_1-C_6 alkylacyloxy,

(7) amido

(8) C_1-C_6 alkylamino

(9) phenylamino,

(10) carbamyl

(11) carboxyl

(12) carboxy(C_2-C_5)alkoxy,

(13) carboxy(C_2-C5)alkylthioxy,

(14) heterocyclylacyl,

(15) heteroarylacyl,

(16) amino unsubstituted or substituted with C_1-C_6 alkyl,

(17) hydroxyl, or

(18) carboxyl methyl ester;

(II)-$(CH_2)_{0-3}$-J-[(-$(CH_2)_{0-3}$-K]$_{1-3}$ where K is as defined above and J is:

(A) a 5 to 7 atom monocyclic aryl group,

(B) a 8 to 12 atom multicyclic aryl group,

(C) a 5 to 7 atom heterocyclic group,

(D) a 8 to 12 atom multicyclic heterocyclic group, or

(E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -$(CH_2)_{0-3}$-(C_3-C_7) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

(A) C_1-C_3 alkyl unsubstituted or substituted with 1, 2, 3, or 4 –F, -Cl, -Br, or -I,

(B) -CO-OH,

(C) -CO-O-(C_1-C_4 alkyl),

(D) -OH, or

(E) C_1-C_6 alkoxy,

(IV) -$(CH_2)_{2-6}$-OH,

(V) -$(CR_{C-x}R_{C-y})_{0-4}$-R_{C-aryl} where R_{C-x} and R_{C-y} are –H, C_1-C_4 alkyl and ϕ- and R_{C-aryl} is the same as R_{N-aryl},

(VI) -$(CH_2)_{0-4}$-$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) isoxazolyl,

(Q) pyrazolyl,

(R) indolizinyl,

(S) indazolyl,

(T) benzothiazolyl,

(U) benzimidazolyl,

(V) benzofuranyl,

(W) furanyl,

(X) thienyl,

(Y) pyrrolyl,

(Z) oxadiazolyl,

(AA) thiadiazolyl,

(BB) triazolyl,

(CC) tetrazolyl,

(DD) 1, 4-benzodioxan

(EE) purinyl,

(FF) oxazolopyridinyl,

(GG) imidazopyridinyl,

(HH) isothiazolyl,

(II) naphthyridinyl,

(JJ) cinnolinyl,

(KK) carbazolyl,

(LL) β-carbolinyl,

(MM) isochromanyl,

(NN) chromanyl,

(OO) furazanyl,

(PP) tetrahydroisoquinoline,

(QQ) isoindolinyl,

(RR) isobenzotetrahydrofuranyl,

(SS) isobenzotetrahydrothienyl,

(TT) isobenzothiophenyl,

(UU) benzoxazolyl, or

(VV) pyridopyridinyl,

(VII) $-(CH_2)_{0-4}-R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is the same as $R_{1\text{-heterocycle}}$,

(VIII) $-C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3}$ where R_{C-1} and R_{C-2} are the same or different and are:

(A) -H,

(B) $-C_1-C_6$ alkyl,

(C) $-(C_1-C_4$ alkyl$)-R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above for $R_{1\text{-aryl}}$,

(D) $-(C_1-C_4$ alkyl$)-R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above,

(E) $-(C_1-C_4$ alkyl$)-R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(F) $-R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above,

(G) $-R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(H) $-(CH_2)_{1-4}-OH$,

(I) $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C'\text{-aryl}}$ where R_{C-4} is –O-, -S-, -NH- or $-NHR_{C-5}$- where R_{C-5} is C_1-C_6 alkyl, and where $R_{C'\text{-aryl}}$ is as defined above,

(J) $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C\text{-heteroaryl}}$ where R_{C-4} and $R_{C\text{-heteroaryl}}$ are as defined above, or

(K) $-R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above,

and where R_{C-3} is:

(A) -H,

(B) -C_1-C_6 alkyl,

(C) –$R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above,

(D) –$R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above,

(E) –$R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(F) -(C_1-C_4 alkyl)-$R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above,

(G) -(C_1-C_4 alkyl)-$R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above, or

(H) -(C_1-C_4 alkyl)-$R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(IX) -CH(ϕ)$_2$,

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

(A) C_1-C_3 alkyl,

(B) –CF_3,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) -OCF_3,

(F) -NH_2,

(G) -OH, or

(H) -C≡N,

(XI) –CH_2-C≡CH;

(XII) –(CH_2)$_{0\text{-}1}$-CH$R_{C\text{-}5}$-(CH_2)$_{0\text{-}1}$-ϕ where $R_{C\text{-}5}$ is:

(A) –OH, or

(B)-CH_2-OH;

(XIII) –CH(-ϕ)-CO-O(C_1-C_3 alkyl);

(XIV) –CH(-CH_2-OH)-CH(-OH)-ϕ-NO_2;

(XV) –(CH_2)$_2$-O-(CH_2)$_2$-OH;

(XVI) –CH_2-NH-CH_2-CH(-O-CH_2-CH_3)$_2$;

(XVII) -(C_2-C_8) alkynyl; or

(XVIII) –H; or a pharmaceutically acceptable salt thereof.

39. The method of claim 38, wherein said cleavage site is between Met652 and Asp653, numbered for the APP-751 isotype; between Met 671 and Asp 672, numbered for the APP-770 isotype,; between Leu596 and Asp597 of the APP-695 Swedish Mutation; between Leu652 and Asp653 of the APP-751 Swedish Mutation; or between Leu671 and Asp672 of the APP-770 Swedish Mutation.

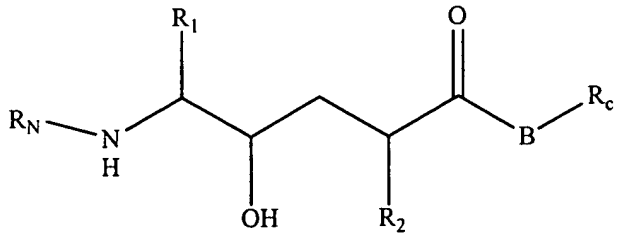
40. The method of claim 38, wherein said reaction mixture is exposed *in vitro*.

41. The method of claim 38, wherein said reaction mixture is exposed in a cell.

42. The method of claim 41, wherein said cell is in an animal.

43. The method of claim 42, wherein said animal is a human.

44. A method for inhibiting production of amyloid beta peptide (Aβ) in a cell, comprising administering to said cell an effective inhibitory amount of a hydroxyethylene compound of the formula



(XII)

where R_1 is:

(I) C_1-C_6 alkyl, unsubstituted or substituted with one, two or three C_1-C_3 alkyl, –F, -Cl, -Br, -I, -OH, $-NH_2$, -C≡N, $-CF_3$, or $-N_3$,

(II) $-(CH_2)_{1-2}$-S-CH_3,

(III) $-CH_2$-CH_2-S-CH_3,

(IV) $-CH_2$-(C_2-C_6 alkenyl) unsubstituted or substituted by one –F,

(V) $-(CH_2)_{0-3}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or

substituted on the aryl ring with one or two of the following substituents which can be the same or different:

(A) C_1-C_3 alkyl,

(B) $-CF_3$,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) $-O-CF_3$,

(F) $-NH_2$,

(G) -OH, or

(H) -C≡N,

(VI) $-(CH_2)_{n1}-(R_{1\text{-heteroaryl}})$ where n_1 is 0, 1, 2, or 3 and $R_{1\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{1\text{-heteroaryl}}$ group is bonded to $-(CH_2)_{0\text{-}3}-$ by any ring atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_3 alkyl,

(2) $-CF_3$,

(3) -F, Cl, -Br, or –I,

(4) C_1-C_3 alkoxy,

(5) $-O-CF_3$,

(6) $-NH_2$,

(7) -OH, or

(8) -C≡N,

with the proviso that when n_1 is zero $R_{1\text{-heteroaryl}}$ is not bonded to the carbon chain by nitrogen, or

(VII) $-(CH_2)_{n1}-(R_{1\text{-heterocycle}})$ where n_1 is as defined above and

$R_{1\text{-heterocycle}}$ is:

(A) morpholinyl,

(B) thiomorpholinyl,

(C) thiomorpholinyl S-oxide,

(D) thiomorpholinyl S,S-dioxide,

(E) piperazinyl,

(F) homopiperazinyl,

(G) pyrrolidinyl,

(H) pyrrolinyl,

(I) tetrahydropyranyl,

(J) piperidinyl,

(K) tetrahydrofuranyl, or

(L) tetrahydrothiophenyl,

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or

two:

(1) =O,

(2) C_1-C_3 alkyl,

(3) $-CF_3$,

(4) -F, Cl, -Br and –I,

(5) C_1-C_3 alkoxy,

(6) $-O-CF_3$,

(7) $-NH_2$,

(8) -OH, or

(9) -C≡N,

with the proviso that when n_1 is zero $R_{1\text{-heterocycle}}$ is not bonded to the carbon chain by nitrogen;

where R_2 is:

(I) -H,

(II) C_1-C_6 alkyl, or

(III) $-(CH_2)_{0-4}-R_{2-1}$ where R_{2-1} is (C_3-C_6)cycloalkyl, $R_{1\text{-aryl}}$ or $R_{1\text{-heteroaryl}}$ where $R_{1\text{-aryl}}$ and $R_{1\text{-heteroaryl}}$ are as defined above,

where R_N is:

(I) R_{N-1}-X_N- where X_N is:

(A) –CO-,

(B) $-SO_2-$,

(C) $-(CR'R'')_{1-6}$ where R' and R" are the same or different and are –H or C_1-C_4 alkyl,

(D) $-CO-(CR'R'')_{1-6}-X_{N-1}$ where X_{N-1} is –O-, -S- and –NR'R"- and where R' and R" are as defined above,

(E) a single bond;

where R_{N-1} is:

(A) $R_{N\text{-aryl}}$ where $R_{N\text{-aryl}}$ is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or -I,

(3) -OH,

(4) $-NO_2$,

(5) -CO-OH,

(6) -C≡N,

(7) -CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) -C_1-C_6 alkyl unsubstituted or substituted with one to three –F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e) -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-R_{N-4} where R_{N-4} is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each

group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-R_{N-5} where R_{N-5} is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0-2}$-(R_{1-aryl}) where R_{1-aryl} is as defined above,

(14) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) -SO_2-(C_3-C_{12} alkyl),

(17) -NH-CO-O-R_{N-5} where R_{N-5} is as defined above,

(18) -NH-CO-N(C_1-C_3 alkyl)$_2$,

(19) -N-CS-N(C_1-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-R_{N-5} where R_{N-5} is as defined above,

(21) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(22) -R_{N-4} where R_{N-4} is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH,

(28) -S-(C_1-C_6 alkyl),

(29) C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F,

(30) –O-(C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F, or

(31) –O-ϕ,

(B) -$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{N\text{-heteroaryl}}$ group is bonded by any atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{N\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or - I,

(3) -OH,

(4) $-NO_2$,

(5) -CO-OH,

(6) -C≡N,

(7) $-CO-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) -NH_2,

(c) -C_1-C_6 alkyl unsubstituted or substituted with 1, 2, or 3 –F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0-2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) -SO_2-(C_3-C_{12} alkyl),

(17) -NH-CO-O-R_{N-5} where R_{N-5} is as defined above,

(18) -NH-CO-N(C_1-C_3 alkyl)$_2$,

(19) -N-CS-N(C_1-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-R_{N-5} where R_{N-5} is as defined above,

(21) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(22) -R_{N-4} where R_{N-4} is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH, or

(28) -S-(C_1-C_6 alkyl),

(C) -$R_{N\text{-aryl}}$-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(D) -$R_{N\text{-aryl}}$-$R_{N\text{-heteroaryl}}$ where -$R_{N\text{-aryl}}$ and -$R_{N\text{-heteroaryl}}$ are as defined above,

(E) -$R_{N\text{-heteroaryl}}$-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ and -$R_{N\text{-heteroaryl}}$ are as defined above,

(F) -$R_{N\text{-heteroaryl}}$-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(G) -$R_{N\text{-aryl}}$-O-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(H) -$R_{N\text{-aryl}}$-S-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(I) -$R_{N\text{-heteroaryl}}$-O-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(J) -$R_{N\text{-heteroaryl}}$-S-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(K) -$R_{N\text{-aryl}}$-CO-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(L) -$R_{N\text{-aryl}}$-CO-$R_{N\text{-heteroaryl}}$ where -$R_{N\text{-aryl}}$ and $R_{N\text{-heteroaryl}}$ are as defined above,

(M) -$R_{N\text{-aryl}}$-SO_2-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(N) -$R_{N\text{-heteroaryl}}$-CO-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(O) -$R_{N\text{-heteroaryl}}$-SO_2-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(P) –$R_{N\text{-aryl}}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-aryl}}$ is as defined above,

(Q) –$R_{N\text{-aryl}}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-aryl}}$ is as defined above,

(R) –$R_{N\text{-heteroaryl}}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above, or

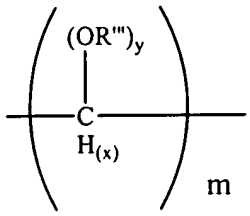
(S) –$R_{N\text{-heteroaryl}}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above,

(II) A-X_N- where X_N is –CO-,

wherein A is

(A) -T-E-$(Q)_{m'}$,

(1) where -T is



where

(a) x =1 when y = 1 and x = 2 when y = 0,

(b) m is 0, 1, 2 or 3,

(c) the values of x and y vary independently on each carbon when m is 2 and 3, and

(d) R'" varies independently on each carbon and is H, (C_1-C_2) alkyl, phenyl, or phenyl(C_1-C_3)alkyl;

(2) -E is

(a) C_1-C_5 alkyl, but only if m' does not equal 0,

(b) methylthioxy(C_2-C_4)alkyl,

(c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,

(f) biphenyl,

(g) diphenyl ether,

(h) diphenylketone,

(i) phenyl(C_1-C_8)alkyloxyphenyl, or

(j) C_1-C_6 alkoxy;

(3) -Q is

(a) C_1-C_3 alkyl,

(b) C_1-C_3 alkoxy,

(c) C_1-C_3 alkylthioxy,

(d) C_1-C_6 alkylacylamino,

(e) C_1-C_6 alkylacyloxy,

(f) amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary amino moieties),

(g) C_1-C_6 alkylamino

(h) phenylamino,

(i) carbamyl (including C_1-C_6 alkyl and phenyl amides and esters),

(j) carboxyl (including C_1-C_6 alkyl and phenyl esters),

(k) carboxy(C_2-C_5)alkoxy,

(l) carboxy(C_2-C5)alkylthioxy,

(m) heterocyclylacyl,

(n) heteroarylacyl, or

(o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) -$E(Q)_{m''}$ wherein E and -Q are as defined as above and m'' is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

(III) –CO-(C_1-C_6 alkyl) where alkyl is unsubstituted or substituted with one or two:

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} is the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(IV) –CO-(C_1-C_3 alkyl)-O-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(V) –CO-(C_1-C_3 alkyl)-S-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) $-SO_2-(C_1-C_8$ alkyl),

(H) $-SO_2-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) $-NH-CO-(C_1-C_6$ alkyl),

(J) $-NH-CO-O-R_{N-8}$ where R_{N-8} is as defined above,

(K) $-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) $-R_{N-4}$ where R_{N-4} is as defined above,

(M) $-O-CO-(C_1-C_6$ alkyl),

(N) $-O-CO-NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) $-O-(C_1-C_5$ alkyl)-COOH,

(VI) $-CO-CH(-(CH_2)_{0-2}-O-R_{N-10})-(CH_2)_{0-2}-R_{N-aryl}/R_{N-heteroaryl}$) where R_{N-aryl} and $R_{N-heteroaryl}$ are as defined above, where R_{N-10} is:

(A) –H,

(B) C_1-C_6 alkyl,

(C) C_3-C_7 cycloalkyl,

(D) C_2-C_6 alkenyl with one double bond,

(E) C_2-C_6 alkynyl with one triple bond,

(F) R_{1-aryl} where R_{1-aryl} is as defined above, or

(G) $R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above;

where B is -O-, -NH-, or $-N(C_1-C_6$ alkyl)-;

where R_C is:

(I) $-(C_1-C_{10})$alkyl-K_{1-3} in which:

(A) the alkyl chain is unsubstituted or substituted with one –OH,

(B) the alkyl chain is unsubstituted or substituted with one C_1-C_6 alkoxy unsubstituted or substituted with 1-5 -F,

(C) the alkyl chain is unsubstituted or substituted with one $-O-\phi$,

(D) the alkyl chain is unsubstituted or substituted with 1-5 –F,

(E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

(1) H,

(2) C_1-C_3 alkyl,

(3) C_1-C_3 alkoxy,

(4) C_1-C_3 alkylthioxy,

(5) C_1-C_6 alkylacylamino,

(6) C_1-C_6 alkylacyloxy,

(7) amido

(8) C_1-C_6 alkylamino

(9) phenylamino,

(10) carbamyl

(11) carboxyl

(12) carboxy(C_2-C_5)alkoxy,

(13) carboxy(C_2-C5)alkylthioxy,

(14) heterocyclylacyl,

(15) heteroarylacyl,

(16) amino unsubstituted or substituted with C_1-C_6 alkyl,

(17) hydroxyl, or

(18) carboxyl methyl ester;

(II)-$(CH_2)_{0-3}$-J-[(-$(CH_2)_{0-3}$-K]$_{1-3}$ where K is as defined above and J is:

(A) a 5 to 7 atom monocyclic aryl group,

(B) a 8 to 12 atom multicyclic aryl group,

(C) a 5 to 7 atom heterocyclic group,

(D) a 8 to 12 atom multicyclic heterocyclic group, or

(E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -$(CH_2)_{0-3}$-$(C_3$-$C_7)$ cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

(A) C_1-C_3 alkyl unsubstituted or substituted with 1, 2, 3, or 4 –F, -Cl, -Br, or -I,

(B) -CO-OH,

(C) -CO-O-(C_1-C_4 alkyl),

(D) -OH, or

(E) C_1-C_6 alkoxy,

(IV) -$(CH_2)_{2-6}$-OH,

(V) -$(CR_{C-x}R_{C-y})_{0-4}$-R_{C-aryl} where R_{C-x} and R_{C-y} are –H, C_1-C_4 alkyl and ϕ- and R_{C-aryl} is the same as R_{N-aryl},

(VI) -$(CH_2)_{0-4}$-$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) isoxazolyl,

(Q) pyrazolyl,

(R) indolizinyl,

(S) indazolyl,

(T) benzothiazolyl,

(U) benzimidazolyl,

(V) benzofuranyl,

(W) furanyl,

(X) thienyl,

(Y) pyrrolyl,

(Z) oxadiazolyl,

(AA) thiadiazolyl,

(BB) triazolyl,

(CC) tetrazolyl,

(DD) 1, 4-benzodioxan

(EE) purinyl,

(FF) oxazolopyridinyl,

(GG) imidazopyridinyl,

(HH) isothiazolyl,

(II) naphthyridinyl,

(JJ) cinnolinyl,

(KK) carbazolyl,

(LL) β-carbolinyl,

(MM) isochromanyl,

(NN) chromanyl,

(OO) furazanyl,

(PP) tetrahydroisoquinoline,

(QQ) isoindolinyl,

(RR) isobenzotetrahydrofuranyl,

(SS) isobenzotetrahydrothienyl,

(TT) isobenzothiophenyl,

(UU) benzoxazolyl, or

(VV) pyridopyridinyl,

(VII) $-(CH_2)_{0-4}-R_{C\text{-}heterocycle}$ where $R_{C\text{-}heterocycle}$ is the same as $R_{1\text{-}heterocycle}$,

(VIII) -C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3} where R_{C-1} and R_{C-2} are the same or different and are:

(A) -H,

(B) -C_1-C_6 alkyl,

(C) -(C_1-C_4 alkyl)-$R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above for R_{1-aryl},

(D) -(C_1-C_4 alkyl)-$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,

(E) -(C_1-C_4 alkyl)-$R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,

(F) –$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,

(G) –$R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,

(H) –$(CH_2)_{1-4}$-OH,

(I) -$(CH_2)_{1-4}$-R_{C-4}-$(CH_2)_{1-4}$-$R_{C'-aryl}$ where R_{C-4} is –O-, -S-, -NH- or –NHR_{C-5}- where R_{C-5} is C_1-C_6 alkyl, and where $R_{C'-aryl}$ is as defined above,

(J) -$(CH_2)_{1-4}$-R_{C-4}-$(CH_2)_{1-4}$-$R_{C-heteroaryl}$ where R_{C-4} and $R_{C-heteroaryl}$ are as defined above, or

(K) –$R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above,

and where R_{C-3} is:

(A) -H,

(B) -C_1-C_6 alkyl,

(C) –$R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above,

(D) –$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,

(E) –$R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,

(F) -(C_1-C_4 alkyl)-$R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above,

(G) -(C_1-C_4 alkyl)-$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above, or

(H) -(C_1-C_4 alkyl)-$R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,

(IX) -CH(ϕ)$_2$,

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

(A) C_1-C_3 alkyl,

(B) $-CF_3$,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) $-OCF_3$,

(F) $-NH_2$,

(G) -OH, or

(H) $-C\equiv N$,

(XI) $-CH_2-C\equiv CH$;

(XII) $-(CH_2)_{0-1}-CHR_{C-5}-(CH_2)_{0-1}-\phi$ where R_{C-5} is:

(A) –OH, or

(B)$-CH_2-OH$;

(XIII) $-CH(-\phi)-CO-O(C_1-C_3$ alkyl);

(XIV) $-CH(-CH_2-OH)-CH(-OH)-\phi-NO_2$;

(XV) $-(CH_2)_2-O-(CH_2)_2-OH$;

(XVI) $-CH_2-NH-CH_2-CH(-O-CH_2-CH_3)_2$;

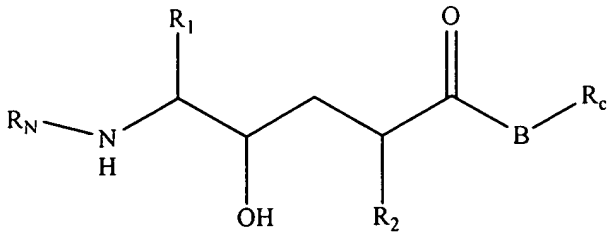
(XVII) $-(C_2-C_8)$ alkynyl; or

(XVIII) –H; or a pharmaceutically acceptable salt thereof.

45. The method of claim 44, wherein said administering is to and animal.

46. The method of claim 45, whererin said administering is to a human.

47. A method for inhibiting the production of beta-amyloid plaque in an animal, comprising administering to said animal an effective inhibitory amount of a hydroxyethylene compound of the formula



(XII)

where R_1 is:

(I) C_1-C_6 alkyl, unsubstituted or substituted with one, two or three C_1-C_3 alkyl, –F, -Cl, -Br, -I, -OH, $-NH_2$, -C≡N, $-CF_3$, or $-N_3$,

(II) $-(CH_2)_{1-2}$-S-CH_3,

(III) $-CH_2$-CH_2-S-CH_3,

(IV) $-CH_2$-(C_2-C_6 alkenyl) unsubstituted or substituted by one –F,

(V) $-(CH_2)_{0-3}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:

(A) C_1-C_3 alkyl,

(B) $-CF_3$,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) –O-CF_3,

(F) $-NH_2$,

(G) -OH, or

(H) -C≡N,

(VI) $-(CH_2)_{n1}$-($R_{1\text{-heteroaryl}}$) where n_1 is 0, 1, 2, or 3 and $R_{1\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{1\text{-heteroaryl}}$ group is bonded to $-(CH_2)_{0\text{-}3}-$ by any ring atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_3 alkyl,

(2) $-CF_3$,

(3) -F, Cl, -Br, or –I,

(4) C_1-C_3 alkoxy,

(5) $-O-CF_3$,

(6) $-NH_2$,

(7) -OH, or

(8) -C≡N,

with the proviso that when n_1 is zero $R_{1\text{-heteroaryl}}$ is not bonded to the carbon chain by nitrogen, or

(VII) $-(CH_2)_{n1}-(R_{1\text{-heterocycle}})$ where n_1 is as defined above and

$R_{1\text{-heterocycle}}$ is:

(A) morpholinyl,

(B) thiomorpholinyl,

(C) thiomorpholinyl S-oxide,

(D) thiomorpholinyl S,S-dioxide,

(E) piperazinyl,

(F) homopiperazinyl,

(G) pyrrolidinyl,

(H) pyrrolinyl,

(I) tetrahydropyranyl,

(J) piperidinyl,

(K) tetrahydrofuranyl, or

(L) tetrahydrothiophenyl,

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

(1) =O,

(2) C_1-C_3 alkyl,

(3) $-CF_3$,

(4) -F, Cl, -Br and –I,

(5) C_1-C_3 alkoxy,

(6) $-O-CF_3$,

(7) $-NH_2$,

(8) -OH, or

(9) -C≡N,

with the proviso that when n_1 is zero $R_{1\text{-heterocycle}}$ is not bonded to the carbon chain by nitrogen;

where R_2 is:

(I) -H,

(II) C_1-C_6 alkyl, or

(III) $-(CH_2)_{0\text{-}4}-R_{2\text{-}1}$ where $R_{2\text{-}1}$ is (C_3-C_6)cycloalkyl, $R_{1\text{-aryl}}$ or $R_{1\text{-heteroaryl}}$ where $R_{1\text{-aryl}}$ and $R_{1\text{-heteroaryl}}$ are as defined above,

where R_N is:

(I) R_{N-1}-X_N- where X_N is:

(A) –CO-,

(B) $-SO_2-$,

(C) $-(CR'R'')_{1-6}$ where R' and R" are the same or different and are –H or C_1-C_4 alkyl,

(D) $-CO-(CR'R'')_{1-6}-X_{N-1}$ where X_{N-1} is –O-, -S- and –NR'R"- and where R' and R" are as defined above,

(E) a single bond;

where R_{N-1} is:

(A) $R_{N\text{-}aryl}$ where $R_{N\text{-}aryl}$ is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or -I,

(3) -OH,

(4) $-NO_2$,

(5) -CO-OH,

(6) -C≡N,

(7) $-CO-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are:

(a) -H,

(b) $-C_1$-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) $-C_1$-C_6 alkyl unsubstituted or substituted with one to three –F, -Cl, -Br, or -I,

(d) $-C_3$-C_7 cycloalkyl,

(e) $-(C_1$-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0\text{-}2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) -SO_2-$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) -SO_2-(C_3-C_{12} alkyl),

(17) -NH-CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(18) -NH-CO-N(C_1-C_3 alkyl)$_2$,

(19) -N-CS-N(C_1-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(21) -$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ can be the same or different and are as defined above,

(22) -$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH,

(28) -S-(C_1-C_6 alkyl),

(29) C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F,

(30) –O-(C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F, or

(31) –O-ϕ,

(B) -$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{N\text{-heteroaryl}}$ group is bonded by any atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{N\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or - I,

(3) -OH,

(4) $-NO_2$,

(5) -CO-OH,

(6) -C≡N,

(7) $-CO-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) -C_1-C_6 alkyl unsubstituted or substituted with 1, 2, or 3 –F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) $-R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above,

or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0\text{-}2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) -SO_2-$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) -SO_2-(C_3-C_{12} alkyl),

(17) -NH-CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(18) -NH-CO-N(C_1-C_3 alkyl)$_2$,

(19) -N-CS-N(C_1-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(21) -$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ can be the same or different and are as defined above,

(22) -$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH, or

(28) -S-(C_1-C_6 alkyl),

(C) -$R_{N\text{-aryl}}$-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(D) -$R_{N\text{-aryl}}$-$R_{N\text{-heteroaryl}}$ where -$R_{N\text{-aryl}}$ and -$R_{N\text{-heteroaryl}}$ are as defined above,

(E) -$R_{N\text{-heteroaryl}}$-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ and -$R_{N\text{-heteroaryl}}$ are as defined above,

(F) -$R_{N\text{-heteroaryl}}$-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(G) -$R_{N\text{-aryl}}$-O-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(H) -$R_{N\text{-aryl}}$-S-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(I) -$R_{N\text{-heteroaryl}}$-O-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(J) -$R_{N\text{-heteroaryl}}$-S-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(K) -$R_{N\text{-aryl}}$-CO-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(L) -$R_{N\text{-aryl}}$-CO-$R_{N\text{-heteroaryl}}$ where -$R_{N\text{-aryl}}$ and $R_{N\text{-heteroaryl}}$ are as defined above,

(M) -$R_{N\text{-aryl}}$-SO_2-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(N) -$R_{N\text{-heteroaryl}}$-CO-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(O) -$R_{N\text{-heteroaryl}}$-SO_2-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(P) –$R_{N\text{-aryl}}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-aryl}}$ is as defined above,

(Q) –$R_{N\text{-aryl}}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-aryl}}$ is as defined above,

(R) –$R_{N\text{-heteroaryl}}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above, or

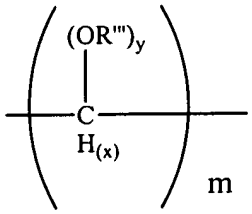
(S) –$R_{N\text{-heteroaryl}}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above,

(II) A-X_N- where X_N is –CO-,

wherein A is

(A) -T-E-$(Q)_{m'}$,

(1) where -T is



where

(a) x =1 when y = 1 and x = 2 when y = 0,

(b) m is 0, 1, 2 or 3,

(c) the values of x and y vary independently on each carbon when m is 2 and 3, and

(d) R'" varies independently on each carbon and is H, (C_1-C_2) alkyl, phenyl, or phenyl(C_1-C_3)alkyl;

(2) -E is

(a) C_1-C_5 alkyl, but only if m' does not equal 0,

(b) methylthioxy(C_2-C_4)alkyl,

(c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,

(f) biphenyl,

(g) diphenyl ether,

(h) diphenylketone,

(i) phenyl(C_1-C_8)alkyloxyphenyl, or

(j) C_1-C_6 alkoxy;

(3) -Q is

(a) C_1-C_3 alkyl,

(b) C_1-C_3 alkoxy,

(c) C_1-C_3 alkylthioxy,

(d) C_1-C_6 alkylacylamino,

(e) C_1-C_6 alkylacyloxy,

(f) amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary amino moieties),

(g) C_1-C_6 alkylamino

(h) phenylamino,

(i) carbamyl (including C_1-C_6 alkyl and phenyl amides and esters),

(j) carboxyl (including C_1-C_6 alkyl and phenyl esters),

(k) carboxy(C_2-C_5)alkoxy,

(l) carboxy(C_2-C5)alkylthioxy,

(m) heterocyclylacyl,

(n) heteroarylacyl, or

(o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) $-E(Q)_{m''}$ wherein E and -Q are as defined as above and m'' is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

(III) –CO-(C_1-C_6 alkyl) where alkyl is unsubstituted or substituted with one or two:

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} is the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(IV) –CO-(C_1-C_3 alkyl)-O-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(V) –CO-(C_1-C_3 alkyl)-S-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(VI) –CO-CH(-$(CH_2)_{0-2}$-O-R_{N-10})-$(CH_2)_{0-2}$-$R_{N\text{-}aryl}$/$R_{N\text{-}heteroaryl}$) where $R_{N\text{-}aryl}$ and $R_{N\text{-}heteroaryl}$ are as defined above, where R_{N-10} is:

(A) –H,

(B) C_1-C_6 alkyl,

(C) C_3-C_7 cycloalkyl,

(D) C_2-C_6 alkenyl with one double bond,

(E) C_2-C_6 alkynyl with one triple bond,

(F) $R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(G) $R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above;

where B is -O-, -NH-, or -N(C_1-C_6 alkyl)-;

where R_C is:

(I) -(C_1-C_{10})alkyl-$K_{1\text{-}3}$ in which:

(A) the alkyl chain is unsubstituted or substituted with one –OH,

(B) the alkyl chain is unsubstituted or substituted with one C_1-C_6 alkoxy unsubstituted or substituted with 1-5 -F,

(C) the alkyl chain is unsubstituted or substituted with one –O-ϕ,

(D) the alkyl chain is unsubstituted or substituted with 1-5 –F,

(E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

(1) H,

(2) C_1-C_3 alkyl,

(3) C_1-C_3 alkoxy,

(4) C_1-C_3 alkylthioxy,

(5) C_1-C_6 alkylacylamino,

(6) C_1-C_6 alkylacyloxy,

(7) amido

(8) C_1-C_6 alkylamino

(9) phenylamino,

(10) carbamyl

(11) carboxyl

(12) carboxy(C_2-C_5)alkoxy,

(13) carboxy(C_2-C5)alkylthioxy,

(14) heterocyclylacyl,

(15) heteroarylacyl,

(16) amino unsubstituted or substituted with C_1-C_6 alkyl,

(17) hydroxyl, or

(18) carboxyl methyl ester;

(II)-$(CH_2)_{0-3}$-J-[(-$(CH_2)_{0-3}$-K]$_{1-3}$ where K is as defined above and J is:

(A) a 5 to 7 atom monocyclic aryl group,

(B) a 8 to 12 atom multicyclic aryl group,

(C) a 5 to 7 atom heterocyclic group,

(D) a 8 to 12 atom multicyclic heterocyclic group, or

(E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -$(CH_2)_{0-3}$-(C_3-C_7) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

(A) C_1-C_3 alkyl unsubstituted or substituted with 1, 2, 3, or 4 –F, -Cl, -Br, or -I,

(B) -CO-OH,

(C) -CO-O-(C_1-C_4 alkyl),

(D) -OH, or

(E) C_1-C_6 alkoxy,

(IV) -$(CH_2)_{2-6}$-OH,

(V) -$(CR_{C-x}R_{C-y})_{0-4}$-R_{C-aryl} where R_{C-x} and R_{C-y} are –H, C_1-C_4 alkyl and ϕ- and R_{C-aryl} is the same as R_{N-aryl},

(VI) -$(CH_2)_{0-4}$-$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) isoxazolyl,

(Q) pyrazolyl,

(R) indolizinyl,

(S) indazolyl,

(T) benzothiazolyl,

(U) benzimidazolyl,

(V) benzofuranyl,

(W) furanyl,

(X) thienyl,

(Y) pyrrolyl,

(Z) oxadiazolyl,

(AA) thiadiazolyl,

(BB) triazolyl,

(CC) tetrazolyl,

(DD) 1, 4-benzodioxan

(EE) purinyl,

(FF) oxazolopyridinyl,

(GG) imidazopyridinyl,

(HH) isothiazolyl,

(II) naphthyridinyl,

(JJ) cinnolinyl,

(KK) carbazolyl,

(LL) β-carbolinyl,

(MM) isochromanyl,

(NN) chromanyl,

(OO) furazanyl,

(PP) tetrahydroisoquinoline,

(QQ) isoindolinyl,

(RR) isobenzotetrahydrofuranyl,

(SS) isobenzotetrahydrothienyl,

(TT) isobenzothiophenyl,

(UU) benzoxazolyl, or

(VV) pyridopyridinyl,

(VII) $-(CH_2)_{0-4}-R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is the same as $R_{1\text{-heterocycle}}$,

(VIII) $-C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3}$ where R_{C-1} and R_{C-2} are the same or different and are:

(A) -H,

(B) $-C_1-C_6$ alkyl,

(C) $-(C_1-C_4$ alkyl$)-R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above for $R_{1\text{-aryl}}$,

(D) $-(C_1-C_4$ alkyl$)-R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above,

(E) $-(C_1-C_4$ alkyl$)-R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(F) $-R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above,

(G) $-R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(H) $-(CH_2)_{1-4}$-OH,

(I) $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C'\text{-aryl}}$ where R_{C-4} is –O-, -S-, -NH- or $-NHR_{C-5}$- where R_{C-5} is C_1-C_6 alkyl, and where $R_{C'\text{-aryl}}$ is as defined above,

(J) $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C\text{-heteroaryl}}$ where R_{C-4} and $R_{C\text{-heteroaryl}}$ are as defined above, or

(K) $-R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above,

and where R_{C-3} is:

(A) -H,

(B) -C_1-C_6 alkyl,

(C) –$R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above,

(D) –$R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above,

(E) –$R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(F) -(C_1-C_4 alkyl)-$R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above,

(G) -(C_1-C_4 alkyl)-$R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above, or

(H) -(C_1-C_4 alkyl)-$R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(IX) -CH(ϕ)$_2$,

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

(A) C_1-C_3 alkyl,

(B) –CF_3,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) -OCF_3,

(F) -NH_2,

(G) -OH, or

(H) -C≡N,

(XI) –CH_2-C≡CH;

(XII) –$(CH_2)_{0\text{-}1}$-$CHR_{C\text{-}5}$-$(CH_2)_{0\text{-}1}$-ϕ where $R_{C\text{-}5}$ is:

(A) –OH, or

(B)-CH_2-OH;

(XIII) –CH(-ϕ)-CO-O(C_1-C_3 alkyl);

(XIV) –CH(-CH_2-OH)-CH(-OH)-ϕ-NO_2;

(XV) –$(CH_2)_2$-O-$(CH_2)_2$-OH;

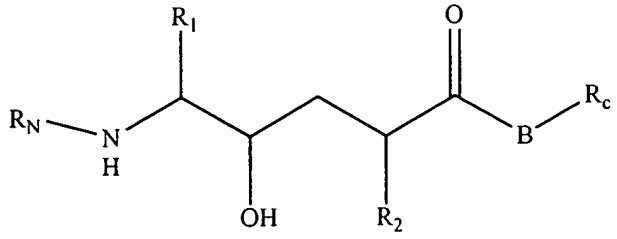
(XVI) –CH_2-NH-CH_2-CH(-O-CH_2-CH_3)$_2$;

(XVII) -(C_2-C_8) alkynyl; or

(XVIII) –H; or a pharmaceutically acceptable salt thereof.

48. The method of claim 47, wherein said animal is a human.

49. A method for treating or preventing a disease characterized by beta-amyloid deposits in the brain comprising administering to a patient an effective therapeutic amount of a hydroxyethylene compound of the formula



(XII)

where R_1 is:

(I) C_1-C_6 alkyl, unsubstituted or substituted with one, two or three C_1-C_3 alkyl, –F, -Cl, -Br, -I, -OH, $-NH_2$, -C≡N, $-CF_3$, or $-N_3$,

(II) $-(CH_2)_{1-2}$-S-CH_3,

(III) $-CH_2$-CH_2-S-CH_3,

(IV) $-CH_2$-(C_2-C_6 alkenyl) unsubstituted or substituted by one –F,

(V) $-(CH_2)_{0-3}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:

(A) C_1-C_3 alkyl,

(B) $-CF_3$,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) –O-CF_3,

(F) $-NH_2$,

(G) -OH, or

(H) -C≡N,

(VI) $-(CH_2)_{n1}$-($R_{1\text{-heteroaryl}}$) where n_1 is 0, 1, 2, or 3 and $R_{1\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{1\text{-heteroaryl}}$ group is bonded to $-(CH_2)_{0\text{-}3}$- by any ring atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_3 alkyl,

(2) $-CF_3$,

(3) -F, Cl, -Br, or –I,

(4) C_1-C_3 alkoxy,

(5) $-O-CF_3$,

(6) $-NH_2$,

(7) -OH, or

(8) -C≡N,

with the proviso that when n_1 is zero $R_{1\text{-heteroaryl}}$ is not bonded to the carbon chain by nitrogen, or

(VII) $-(CH_2)_{n1}-(R_{1\text{-heterocycle}})$ where n_1 is as defined above and

$R_{1\text{-heterocycle}}$ is:

(A) morpholinyl,

(B) thiomorpholinyl,

(C) thiomorpholinyl S-oxide,

(D) thiomorpholinyl S,S-dioxide,

(E) piperazinyl,

(F) homopiperazinyl,

(G) pyrrolidinyl,

(H) pyrrolinyl,

(I) tetrahydropyranyl,

(J) piperidinyl,

(K) tetrahydrofuranyl, or

(L) tetrahydrothiophenyl,

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

(1) =O,

(2) C_1-C_3 alkyl,

(3) $-CF_3$,

(4) -F, Cl, -Br and –I,

(5) C_1-C_3 alkoxy,

(6) $-O-CF_3$,

(7) $-NH_2$,

(8) -OH, or

(9) -C≡N,

with the proviso that when n_1 is zero $R_{1\text{-heterocycle}}$ is not bonded to the carbon chain by nitrogen;

where R_2 is:

(I) -H,

(II) C_1-C_6 alkyl, or

(III) -$(CH_2)_{0-4}$-R_{2-1} where R_{2-1} is (C_3-C_6)cycloalkyl, $R_{1\text{-aryl}}$ or $R_{1\text{-heteroaryl}}$ where $R_{1\text{-aryl}}$ and $R_{1\text{-heteroaryl}}$ are as defined above,

where R_N is:

(I) R_{N-1}-X_N- where X_N is:

(A) –CO-,

(B) –SO_2-,

(C) -$(CR'R'')_{1-6}$ where R' and R" are the same or different and are –H or C_1-C_4 alkyl,

(D) –CO-$(CR'R'')_{1-6}$-X_{N-1} where X_{N-1} is –O-, -S- and –NR'R"- and where R' and R" are as defined above,

(E) a single bond;

where R_{N-1} is:

(A) $R_{N\text{-aryl}}$ where $R_{N\text{-aryl}}$ is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or -I,

(3) -OH,

(4) -NO_2,

(5) -CO-OH,

(6) -C≡N,

(7) -CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) $-C_1$-C_6 alkyl unsubstituted or substituted with one to three –F, -Cl, -Br, or -I,

(d) $-C_3$-C_7 cycloalkyl,

(e) $-(C_1$-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) $-(C_1$-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) $-C_1$-C_6 alkenyl with one or two double bonds,

(h) $-C_1$-C_6 alkynyl with one or two triple bonds,

(i) $-C_1$-C_6 alkyl chain with one double bond and one triple bond,

(j) $-R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) $-R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) $-CO-(C_3$-C_{12} alkyl),

(9) $-CO-(C_3$-C_6 cycloalkyl),

(10) $-CO-R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) $-CO-R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) $-CO-R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) $-CO-O-R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) $-(CH_2)_{0\text{-}2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) $-SO_2-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined above,

(15) $-SO-(C_1$-C_8 alkyl),

(16) $-SO_2$-(C_3-C_{12} alkyl),

(17) $-NH-CO-O-R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(18) $-NH-CO-N(C_1$-C_3 alkyl)$_2$,

(19) $-N-CS-N(C_1$-C_3 alkyl)$_2$,

(20) $-N(C_1\text{-}C_3$ alkyl)-CO-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(21) -$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ can be the same or different and are as defined above,

(22) -$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-$N(C_1\text{-}C_3$ alkyl)$_2$,

(25) -O-CS-$N(C_1\text{-}C_3$ alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH,

(28) -S-(C_1-C_6 alkyl),

(29) C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F,

(30) –O-(C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F, or

(31) –O-ϕ,

(B) -$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{N\text{-heteroaryl}}$ group is bonded by any atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{N\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or - I,

(3) -OH,

(4) $-NO_2$,

(5) -CO-OH,

(6) -C≡N,

(7) $-CO-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) -C_1-C_6 alkyl unsubstituted or substituted with 1, 2, or 3 –F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0\text{-}2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) -SO_2-$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) -SO_2-(C_3-C_{12} alkyl),

(17) -NH-CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(18) -NH-CO-N(C_1-C_3 alkyl)$_2$,

(19) -N-CS-N(C_1-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-R_{N-5} where R_{N-5} is as defined above,

(21) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(22) -R_{N-4} where R_{N-4} is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH, or

(28) -S-(C_1-C_6 alkyl),

(C) -R_{N-aryl}-R_{N-aryl} where -R_{N-aryl} is as defined above,

(D) -R_{N-aryl}-$R_{N-heteroaryl}$ where -R_{N-aryl} and -$R_{N-heteroaryl}$ are as defined above,

(E) -$R_{N-heteroaryl}$-R_{N-aryl} where -R_{N-aryl} and -$R_{N-heteroaryl}$ are as defined above,

(F) -$R_{N-heteroaryl}$-$R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above,

(G) -R_{N-aryl}-O-R_{N-aryl} where -R_{N-aryl} is as defined above,

(H) -R_{N-aryl}-S-R_{N-aryl} where -R_{N-aryl} is as defined above,

(I) -$R_{N-heteroaryl}$-O-$R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above,

(J) -$R_{N-heteroaryl}$-S-$R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above,

(K) -R_{N-aryl}-CO-R_{N-aryl} where -R_{N-aryl} is as defined above,

(L) -R_{N-aryl}-CO-$R_{N-heteroaryl}$ where -R_{N-aryl} and $R_{N-heteroaryl}$ are as defined above,

(M) -R_{N-aryl}-SO_2-R_{N-aryl} where -R_{N-aryl} is as defined above,

(N) -$R_{N-heteroaryl}$-CO-$R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above,

(O) -$R_{N-heteroaryl}$-SO_2-$R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above,

(P) –R_{N-aryl}-O-(C_1-C_8 alkyl)-ϕ where R_{N-aryl} is as defined above,

(Q) –R_{N-aryl}-S-(C_1-C_8 alkyl)-ϕ where R_{N-aryl} is as defined above,

(R) $-R_{N\text{-heteroaryl}}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above, or

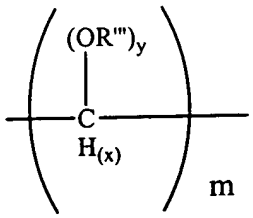
(S) $-R_{N\text{-heteroaryl}}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above,

(II) A-X_N- where X_N is –CO-,

wherein A is

(A) -T-E-$(Q)_{m'}$,

(1) where -T is



where

(a) x =1 when y = 1 and x = 2 when y = 0,

(b) m is 0, 1, 2 or 3,

(c) the values of x and y vary independently on each carbon when m is 2 and 3, and

(d) R'" varies independently on each carbon and is H, (C_1-C_2) alkyl, phenyl, or phenyl(C_1-C_3)alkyl;

(2) -E is

(a) C_1-C_5 alkyl, but only if m' does not equal 0,

(b) methylthioxy(C_2-C_4)alkyl,

(c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,

(f) biphenyl,

(g) diphenyl ether,

(h) diphenylketone,

(i) phenyl(C_1-C_8)alkyloxyphenyl, or

(j) C_1-C_6 alkoxy;

(3) -Q is

(a) C_1-C_3 alkyl,

(b) C_1-C_3 alkoxy,

(c) C_1-C_3 alkylthioxy,

(d) C_1-C_6 alkylacylamino,

(e) C_1-C_6 alkylacyloxy,

(f) amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary amino moieties),

(g) C_1-C_6 alkylamino

(h) phenylamino,

(i) carbamyl (including C_1-C_6 alkyl and phenyl amides and esters),

(j) carboxyl (including C_1-C_6 alkyl and phenyl esters),

(k) carboxy(C_2-C_5)alkoxy,

(l) carboxy(C_2-C5)alkylthioxy,

(m) heterocyclylacyl,

(n) heteroarylacyl, or

(o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) $-E(Q)_{m''}$ wherein E and -Q are as defined as above and m" is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

(III) –CO-(C_1-C_6 alkyl) where alkyl is unsubstituted or substituted with one or two:

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} is the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(IV) –CO-(C_1-C_3 alkyl)-O-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(V) –CO-(C_1-C_3 alkyl)-S-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(VI) –CO-CH(-$(CH_2)_{0-2}$-O-R_{N-10})-$(CH_2)_{0-2}$-$R_{N\text{-}aryl}$/$R_{N\text{-}heteroaryl}$) where $R_{N\text{-}aryl}$ and $R_{N\text{-}heteroaryl}$ are as defined above, where R_{N-10} is:

(A) –H,

(B) C_1-C_6 alkyl,

(C) C_3-C_7 cycloalkyl,

(D) C_2-C_6 alkenyl with one double bond,

(E) C_2-C_6 alkynyl with one triple bond,

(F) $R_{1\text{-}aryl}$ where $R_{1\text{-}aryl}$ is as defined above, or

(G) $R_{N\text{-}heteroaryl}$ where $R_{N\text{-}heteroaryl}$ is as defined above;

where B is -O-, -NH-, or -N(C_1-C_6 alkyl)-;

where R_C is:

(I) -(C_1-C_{10})alkyl-K_{1-3} in which:

(A) the alkyl chain is unsubstituted or substituted with one –OH,

(B) the alkyl chain is unsubstituted or substituted with one C_1-C_6 alkoxy unsubstituted or substituted with 1-5 -F,

(C) the alkyl chain is unsubstituted or substituted with one –O-ϕ,

(D) the alkyl chain is unsubstituted or substituted with 1-5 –F,

(E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

(1) H,

(2) C_1-C_3 alkyl,

(3) C_1-C_3 alkoxy,

(4) C_1-C_3 alkylthioxy,

(5) C_1-C_6 alkylacylamino,

(6) C_1-C_6 alkylacyloxy,

(7) amido

(8) C_1-C_6 alkylamino

(9) phenylamino,

(10) carbamyl

(11) carboxyl

(12) carboxy(C_2-C_5)alkoxy,

(13) carboxy(C_2-C5)alkylthioxy,

(14) heterocyclylacyl,

(15) heteroarylacyl,

(16) amino unsubstituted or substituted with C_1-C_6 alkyl,

(17) hydroxyl, or

(18) carboxyl methyl ester;

(II)-$(CH_2)_{0-3}$-J-[(-$(CH_2)_{0-3}$-K]$_{1-3}$ where K is as defined above and J is:

(A) a 5 to 7 atom monocyclic aryl group,

(B) a 8 to 12 atom multicyclic aryl group,

(C) a 5 to 7 atom heterocyclic group,

(D) a 8 to 12 atom multicyclic heterocyclic group, or

(E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -$(CH_2)_{0-3}$-(C_3-C_7) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

(A) C_1-C_3 alkyl unsubstituted or substituted with 1, 2, 3, or 4 –F, -Cl, -Br, or -I,

(B) -CO-OH,

(C) -CO-O-(C_1-C_4 alkyl),

(D) -OH, or

(E) C_1-C_6 alkoxy,

(IV) -$(CH_2)_{2-6}$-OH,

(V) -$(CR_{C-x}R_{C-y})_{0-4}$-R_{C-aryl} where R_{C-x} and R_{C-y} are –H, C_1-C_4 alkyl and ϕ- and R_{C-aryl} is the same as R_{N-aryl},

(VI) -$(CH_2)_{0-4}$-$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) isoxazolyl,

(Q) pyrazolyl,

(R) indolizinyl,

(S) indazolyl,

(T) benzothiazolyl,

(U) benzimidazolyl,

(V) benzofuranyl,

(W) furanyl,

(X) thienyl,

(Y) pyrrolyl,

(Z) oxadiazolyl,

(AA) thiadiazolyl,

(BB) triazolyl,

(CC) tetrazolyl,

(DD) 1, 4-benzodioxan

(EE) purinyl,

(FF) oxazolopyridinyl,

(GG) imidazopyridinyl,

(HH) isothiazolyl,

(II) naphthyridinyl,

(JJ) cinnolinyl,

(KK) carbazolyl,

(LL) β-carbolinyl,

(MM) isochromanyl,

(NN) chromanyl,

(OO) furazanyl,

(PP) tetrahydroisoquinoline,

(QQ) isoindolinyl,

(RR) isobenzotetrahydrofuranyl,

(SS) isobenzotetrahydrothienyl,

(TT) isobenzothiophenyl,

(UU) benzoxazolyl, or

(VV) pyridopyridinyl,

(VII) $-(CH_2)_{0-4}-R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is the same as $R_{1\text{-heterocycle}}$,

(VIII) $-C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3}$ where R_{C-1} and R_{C-2} are the same or different and are:

(A) -H,

(B) $-C_1-C_6$ alkyl,

(C) $-(C_1-C_4$ alkyl$)-R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above for $R_{1\text{-aryl}}$,

(D) $-(C_1-C_4$ alkyl$)-R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above,

(E) $-(C_1-C_4$ alkyl$)-R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(F) $-R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above,

(G) $-R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(H) $-(CH_2)_{1-4}$-OH,

(I) $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C'\text{-aryl}}$ where R_{C-4} is –O-, -S-, -NH- or

$-NHR_{C\text{-}5}$- where $R_{C\text{-}5}$ is C_1-C_6 alkyl, and where $R_{C'\text{-}aryl}$ is as defined above,

(J) $-(CH_2)_{1\text{-}4}$-$R_{C\text{-}4}$-$(CH_2)_{1\text{-}4}$-$R_{C\text{-}heteroaryl}$ where $R_{C\text{-}4}$ and $R_{C\text{-}heteroaryl}$ are as defined above, or

(K) $-R_{C'\text{-}aryl}$ where $R_{C'\text{-}aryl}$ is as defined above,

and where $R_{C\text{-}3}$ is:

(A) -H,

(B) -C_1-C_6 alkyl,

(C) $-R_{C'\text{-}aryl}$ where $R_{C'\text{-}aryl}$ is as defined above,

(D) $-R_{C\text{-}heteroaryl}$ where $R_{C\text{-}heteroaryl}$ is as defined above,

(E) $-R_{C\text{-}heterocycle}$ where $R_{C\text{-}heterocycle}$ is as defined above,

(F) -(C_1-C_4 alkyl)-$R_{C'\text{-}aryl}$ where $R_{C'\text{-}aryl}$ is as defined above,

(G) -(C_1-C_4 alkyl)-$R_{C\text{-}heteroaryl}$ where $R_{C\text{-}heteroaryl}$ is as defined above, or

(H) -(C_1-C_4 alkyl)-$R_{C\text{-}heterocycle}$ where $R_{C\text{-}heterocycle}$ is as defined above,

(IX) $-CH(\phi)_2$,

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

(A) C_1-C_3 alkyl,

(B) $-CF_3$,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) $-OCF_3$,

(F) $-NH_2$,

(G) -OH, or

(H) -C≡N,

(XI) $-CH_2$-C≡CH;

(XII) $-(CH_2)_{0\text{-}1}$-$CHR_{C\text{-}5}$-$(CH_2)_{0\text{-}1}$-ϕ where $R_{C\text{-}5}$ is:

(A) –OH, or

(B)-CH_2-OH;

(XIII) –CH(-ϕ)-CO-O(C_1-C_3 alkyl);

(XIV) –CH(-CH_2-OH)-CH(-OH)-ϕ-NO_2;

(XV) –$(CH_2)_2$-O-$(CH_2)_2$-OH;

(XVI) –CH_2-NH-CH_2-CH(-O-CH_2-$CH_3)_2$;

(XVII) -(C_2-C_8) alkynyl; or

(XVIII) –H; or a pharmaceutically acceptable salt thereof.

50. The method of claim 49, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 0.1nM to about 200μM.

51. The method of claim 50, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 10nM to about 100μM.

52. The method of claim 51, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 100nM to about 50μM.

53. The method of claim 52, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 1μM to about 10μM.

54. The method of claim 49, wherein said thereapeutic amount is in the range of from about 0.1 to about 1000 mg/day.

55. The method of claim 49, wherein said thereapeutic amount is in the range of from about 15 to about 1500 mg/day.

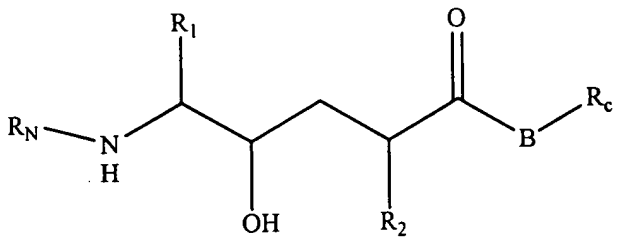
56. The method of claim 55, wherein said thereapeutic amount is in the range of from about 1 to about 100 mg/day.

57. The method of claim 56, wherein said thereapeutic amount is in the range of from about 5 to about 50 mg/day.

58. The method of claim 49, wherein said disease is Alzheimer's disease.

59. The method of claim 49, wherein said disease is Mild Cognitive Impairment, Down's Syndrome, or Hereditary Cerebral Hemmorrhage with Amyloidosis of the Dutch Type.

60. A composition comprising β-secretase complexed with a hydroxyethylene compound of the formula



(XII)

where R_1 is:

(I) C_1-C_6 alkyl, unsubstituted or substituted with one, two or three C_1-C_3 alkyl, –F, -Cl, -Br, -I, -OH, $-NH_2$, -C≡N, $-CF_3$, or $-N_3$,

(II) $-(CH_2)_{1-2}$-S-CH_3,

(III) $-CH_2-CH_2$-S-CH_3,

(IV) $-CH_2$-(C_2-C_6 alkenyl) unsubstituted or substituted by one –F,

(V) $-(CH_2)_{0-3}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:

(A) C_1-C_3 alkyl,

(B) $-CF_3$,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) –O-CF_3,

(F) $-NH_2$,

(G) -OH, or

(H) -C≡N,

(VI) $-(CH_2)_{n1}-(R_{1\text{-heteroaryl}})$ where n_1 is 0, 1, 2, or 3 and $R_{1\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{1\text{-heteroaryl}}$ group is bonded to $-(CH_2)_{0\text{-}3}-$ by any ring atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_3 alkyl,

(2) $-CF_3$,

(3) -F, Cl, -Br, or –I,

(4) C_1-C_3 alkoxy,

(5) $-O-CF_3$,

(6) $-NH_2$,

(7) -OH, or

(8) $-C\equiv N$,

with the proviso that when n_1 is zero $R_{1\text{-heteroaryl}}$ is not bonded to the carbon chain by nitrogen, or

(VII) $-(CH_2)_{n1}-(R_{1\text{-heterocycle}})$ where n_1 is as defined above and

$R_{1\text{-heterocycle}}$ is:

(A) morpholinyl,

(B) thiomorpholinyl,

(C) thiomorpholinyl S-oxide,

(D) thiomorpholinyl S,S-dioxide,

(E) piperazinyl,

(F) homopiperazinyl,

(G) pyrrolidinyl,

(H) pyrrolinyl,

(I) tetrahydropyranyl,

(J) piperidinyl,

(K) tetrahydrofuranyl, or

(L) tetrahydrothiophenyl,

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

(1) =O,

(2) C_1-C_3 alkyl,

(3) $-CF_3$,

(4) -F, Cl, -Br and –I,

(5) C_1-C_3 alkoxy,

(6) $-O-CF_3$,

(7) $-NH_2$,

(8) -OH, or

(9) -C≡N,

with the proviso that when n_1 is zero $R_{1\text{-heterocycle}}$ is not bonded to the carbon chain by nitrogen;

where R_2 is:

(I) -H,

(II) C_1-C_6 alkyl, or

(III) $-(CH_2)_{0\text{-}4}$-$R_{2\text{-}1}$ where $R_{2\text{-}1}$ is (C_3-C_6)cycloalkyl, $R_{1\text{-aryl}}$ or $R_{1\text{-heteroaryl}}$ where $R_{1\text{-aryl}}$ and $R_{1\text{-heteroaryl}}$ are as defined above,

where R_N is:

(I) $R_{N\text{-}1}$-X_N- where X_N is:

(A) –CO-,

(B) $–SO_2$-,

(C) $-(CR'R'')_{1\text{-}6}$ where R' and R" are the same or different and are –H or C_1-C_4 alkyl,

(D) $–CO-(CR'R'')_{1\text{-}6}$-$X_{N\text{-}1}$ where $X_{N\text{-}1}$ is –O-, -S- and –NR'R"- and where R' and R" are as defined above,

(E) a single bond;

where $R_{N\text{-}1}$ is:

(A) $R_{N\text{-aryl}}$ where $R_{N\text{-aryl}}$ is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or -I,

(3) -OH,

(4) $-NO_2$,

(5) -CO-OH,

(6) -C≡N,

(7) $-CO-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) -NH_2,

(c) -C_1-C_6 alkyl unsubstituted or substituted with one to three –F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e) -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0\text{-}2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) -SO_2-$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) -SO_2-(C_3-C_{12} alkyl),

(17) -NH-CO-O-R_{N-5} where R_{N-5} is as defined above,

(18) -NH-CO-N(C_1-C_3 alkyl)$_2$,

(19) -N-CS-N(C_1-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-R_{N-5} where R_{N-5} is as defined above,

(21) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(22) -R_{N-4} where R_{N-4} is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH,

(28) -S-(C_1-C_6 alkyl),

(29) C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F,

(30) –O-(C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F, or

(31) –O-ϕ,

(B) -$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{N\text{-heteroaryl}}$ group is bonded by any atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{N\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or - I,

(3) -OH,

(4) $-NO_2$,

(5) -CO-OH,

(6) -C≡N,

(7) $-CO-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) -C_1-C_6 alkyl unsubstituted or substituted with 1, 2, or 3 –F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0\text{-}2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) -SO_2-$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) -SO_2-(C_3-C_{12} alkyl),

(17) -NH-CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(18) -NH-CO-N(C_1-C_3 alkyl)$_2$,

(19) -N-CS-N(C_1-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is as defined above,

(21) -N$R_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ can be the same or different and are as defined above,

(22) -$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH, or

(28) -S-(C_1-C_6 alkyl),

(C) -$R_{N\text{-aryl}}$-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(D) -$R_{N\text{-aryl}}$-$R_{N\text{-heteroaryl}}$ where -$R_{N\text{-aryl}}$ and -$R_{N\text{-heteroaryl}}$ are as defined above,

(E) -$R_{N\text{-heteroaryl}}$-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ and -$R_{N\text{-heteroaryl}}$ are as defined above,

(F) -$R_{N\text{-heteroaryl}}$-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(G) -$R_{N\text{-aryl}}$-O-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(H) -$R_{N\text{-aryl}}$-S-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(I) -$R_{N\text{-heteroaryl}}$-O-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(J) -$R_{N\text{-heteroaryl}}$-S-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(K) -$R_{N\text{-aryl}}$-CO-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(L) -$R_{N\text{-aryl}}$-CO-$R_{N\text{-heteroaryl}}$ where -$R_{N\text{-aryl}}$ and $R_{N\text{-heteroaryl}}$ are as defined above,

(M) -$R_{N\text{-aryl}}$-SO_2-$R_{N\text{-aryl}}$ where -$R_{N\text{-aryl}}$ is as defined above,

(N) -$R_{N\text{-heteroaryl}}$-CO-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(O) -$R_{N\text{-heteroaryl}}$-SO_2-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(P) –$R_{N\text{-aryl}}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-aryl}}$ is as defined above,

(Q) $-R_{N\text{-}aryl}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-}aryl}$ is as defined above,

(R) $-R_{N\text{-}heteroaryl}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-}heteroaryl}$ is as defined above, or

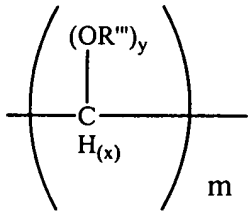
(S) $-R_{N\text{-}heteroaryl}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-}heteroaryl}$ is as defined above,

(II) A-X_N- where X_N is –CO-,

wherein A is

(A) -T-E-$(Q)_{m'}$,

(1) where -T is



where

(a) x =1 when y = 1 and x = 2 when y = 0,

(b) m is 0, 1, 2 or 3,

(c) the values of x and y vary independently on each carbon when m is 2 and 3, and

(d) R'" varies independently on each carbon and is H, (C_1-C_2) alkyl, phenyl, or phenyl(C_1-C_3)alkyl;

(2) -E is

(a) C_1-C_5 alkyl, but only if m' does not equal 0,

(b) methylthioxy(C_2-C_4)alkyl,

(c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,

(f) biphenyl,

(g) diphenyl ether,

(h) diphenylketone,

(i) phenyl(C_1-C_8)alkyloxyphenyl, or

(j) C_1-C_6 alkoxy;

(3) -Q is

(a) C_1-C_3 alkyl,

(b) C_1-C_3 alkoxy,

(c) C_1-C_3 alkylthioxy,

(d) C_1-C_6 alkylacylamino,

(e) C_1-C_6 alkylacyloxy,

(f) amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary amino moieties),

(g) C_1-C_6 alkylamino

(h) phenylamino,

(i) carbamyl (including C_1-C_6 alkyl and phenyl amides and esters),

(j) carboxyl (including C_1-C_6 alkyl and phenyl esters),

(k) carboxy(C_2-C_5)alkoxy,

(l) carboxy(C_2-C5)alkylthioxy,

(m) heterocyclylacyl,

(n) heteroarylacyl, or

(o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) $-E(Q)_{m''}$ wherein E and -Q are as defined as above and m'' is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

(III) –CO-(C_1-C_6 alkyl) where alkyl is unsubstituted or substituted with one or two:

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} is the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(IV) –CO-(C_1-C_3 alkyl)-O-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(V) –CO-(C_1-C_3 alkyl)-S-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(VI) –CO-CH(-$(CH_2)_{0-2}$-O-R_{N-10})-$(CH_2)_{0-2}$-R_{N-aryl}/$R_{N-heteroaryl}$) where R_{N-aryl} and $R_{N-heteroaryl}$ are as defined above, where R_{N-10} is:

(A) –H,

(B) C_1-C_6 alkyl,

(C) C_3-C_7 cycloalkyl,

(D) C_2-C_6 alkenyl with one double bond,

(E) C_2-C_6 alkynyl with one triple bond,

(F) R_{1-aryl} where R_{1-aryl} is as defined above, or

(G) $R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above;

where B is -O-, -NH-, or -N(C_1-C_6 alkyl)-;

where R_C is:

(I) -(C_1-C_{10})alkyl-K_{1-3} in which:

(A) the alkyl chain is unsubstituted or substituted with one –OH,

(B) the alkyl chain is unsubstituted or substituted with one C_1-C_6 alkoxy unsubstituted or substituted with 1-5 -F,

(C) the alkyl chain is unsubstituted or substituted with one –O-ϕ,

(D) the alkyl chain is unsubstituted or substituted with 1-5 –F,

(E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

(1) H,

(2) C_1-C_3 alkyl,

(3) C_1-C_3 alkoxy,

(4) C_1-C_3 alkylthioxy,

(5) C_1-C_6 alkylacylamino,

(6) C_1-C_6 alkylacyloxy,

(7) amido

(8) C_1-C_6 alkylamino

(9) phenylamino,

(10) carbamyl

(11) carboxyl

(12) carboxy(C_2-C_5)alkoxy,

(13) carboxy(C_2-C5)alkylthioxy,

(14) heterocyclylacyl,

(15) heteroarylacyl,

(16) amino unsubstituted or substituted with C_1-C_6 alkyl,

(17) hydroxyl, or

(18) carboxyl methyl ester;

(II)-$(CH_2)_{0-3}$-J-[(-$(CH_2)_{0-3}$-K]$_{1-3}$ where K is as defined above and J is:

(A) a 5 to 7 atom monocyclic aryl group,

(B) a 8 to 12 atom multicyclic aryl group,

(C) a 5 to 7 atom heterocyclic group,

(D) a 8 to 12 atom multicyclic heterocyclic group, or

(E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -$(CH_2)_{0-3}$-(C_3-C_7) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

(A) C_1-C_3 alkyl unsubstituted or substituted with 1, 2, 3, or 4 –F, -Cl, -Br, or -I,

(B) -CO-OH,

(C) -CO-O-(C_1-C_4 alkyl),

(D) -OH, or

(E) C_1-C_6 alkoxy,

(IV) -$(CH_2)_{2-6}$-OH,

(V) -$(CR_{C-x}R_{C-y})_{0-4}$-R_{C-aryl} where R_{C-x} and R_{C-y} are –H, C_1-C_4 alkyl and ϕ- and R_{C-aryl} is the same as R_{N-aryl},

(VI) -$(CH_2)_{0-4}$-$R_{C\text{-}heteroaryl}$ where $R_{C\text{-}heteroaryl}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) isoxazolyl,

(Q) pyrazolyl,

(R) indolizinyl,

(S) indazolyl,

(T) benzothiazolyl,

(U) benzimidazolyl,

(V) benzofuranyl,

(W) furanyl,

(X) thienyl,

(Y) pyrrolyl,

(Z) oxadiazolyl,

(AA) thiadiazolyl,

(BB) triazolyl,

(CC) tetrazolyl,

(DD) 1, 4-benzodioxan

(EE) purinyl,

(FF) oxazolopyridinyl,

(GG) imidazopyridinyl,

(HH) isothiazolyl,

(II) naphthyridinyl,

(JJ) cinnolinyl,

(KK) carbazolyl,

(LL) β-carbolinyl,

(MM) isochromanyl,

(NN) chromanyl,

(OO) furazanyl,

(PP) tetrahydroisoquinoline,

(QQ) isoindolinyl,

(RR) isobenzotetrahydrofuranyl,

(SS) isobenzotetrahydrothienyl,

(TT) isobenzothiophenyl,

(UU) benzoxazolyl, or

(VV) pyridopyridinyl,

(VII) $-(CH_2)_{0-4}-R_{C\text{-}heterocycle}$ where $R_{C\text{-}heterocycle}$ is the same as $R_{1\text{-}heterocycle}$,

(VIII) $-C(R_{C\text{-}1})(R_{C\text{-}2})-CO-NH-R_{C\text{-}3}$ where $R_{C\text{-}1}$ and $R_{C\text{-}2}$ are the same or different and are:

(A) -H,

(B) $-C_1-C_6$ alkyl,

(C) $-(C_1-C_4$ alkyl$)-R_{C'\text{-}aryl}$ where $R_{C'\text{-}aryl}$ is as defined above for $R_{1\text{-}aryl}$,

(D) $-(C_1-C_4$ alkyl$)-R_{C\text{-}heteroaryl}$ where $R_{C\text{-}heteroaryl}$ is as defined above,

(E) $-(C_1-C_4$ alkyl$)-R_{C\text{-}heterocycle}$ where $R_{C\text{-}heterocycle}$ is as defined above,

(F) $-R_{C\text{-}heteroaryl}$ where $R_{C\text{-}heteroaryl}$ is as defined above,

(G) $-R_{C\text{-}heterocycle}$ where $R_{C\text{-}heterocycle}$ is as defined above,

(H) $-(CH_2)_{1-4}$-OH,

(I) -$(CH_2)_{1-4}$-R_{C-4}-$(CH_2)_{1-4}$-$R_{C'-aryl}$ where R_{C-4} is –O-, -S-, -NH- or –NHR_{C-5}- where R_{C-5} is C_1-C_6 alkyl, and where $R_{C'-aryl}$ is as defined above,

(J) -$(CH_2)_{1-4}$-R_{C-4}-$(CH_2)_{1-4}$-$R_{C-heteroaryl}$ where R_{C-4} and $R_{C-heteroaryl}$ are as defined above, or

(K) –$R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above,

and where R_{C-3} is:

(A) -H,

(B) -C_1-C_6 alkyl,

(C) –$R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above,

(D) –$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,

(E) –$R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,

(F) -(C_1-C_4 alkyl)-$R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above,

(G) -(C_1-C_4 alkyl)-$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above, or

(H) -(C_1-C_4 alkyl)-$R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,

(IX) -$CH(\phi)_2$,

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

(A) C_1-C_3 alkyl,

(B) –CF_3,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) -OCF_3,

(F) -NH_2,

(G) -OH, or

(H) -C≡N,

(XI) –CH_2-C≡CH;

(XII) –$(CH_2)_{0-1}$-CHR_{C-5}-$(CH_2)_{0-1}$-ϕ where R_{C-5} is:

(A) –OH, or

(B)-CH_2-OH;

(XIII) –CH(-ϕ)-CO-O(C_1-C_3 alkyl);

(XIV) –CH(-CH_2-OH)-CH(-OH)-ϕ-NO_2;

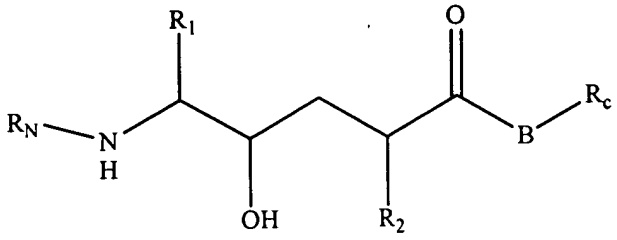
(XV) –$(CH_2)_2$-O-$(CH_2)_2$-OH;

(XVI) –CH_2-NH-CH_2-CH(-O-CH_2-CH_3)$_2$;

(XVII) -(C_2-C_8) alkynyl; or

(XVIII) –H; or a pharmaceutically acceptable salt thereof.

61. A method for producing a β-secretase complex comprising exposing β-secretase to a hydroxyethylene compound of the formula



(XII)

where R_1 is:

(I) C_1-C_6 alkyl, unsubstituted or substituted with one, two or three C_1-C_3 alkyl, –F, -Cl, -Br, -I, -OH, -NH_2, -C≡N, -CF_3, or -N_3,

(II) –$(CH_2)_{1-2}$-S-CH_3,

(III) –CH_2-CH_2-S-CH_3,

(IV) -CH_2-(C_2-C_6 alkenyl) unsubstituted or substituted by one –F,

(V) -$(CH_2)_{0-3}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:

(A) C_1-C_3 alkyl,

(B) –CF_3,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) –O-CF_3,

(F) -NH_2,

(G) -OH, or

(H) -C≡N,

(VI) -$(CH_2)_{n1}$-($R_{1\text{-heteroaryl}}$) where n_1 is 0, 1, 2, or 3 and $R_{1\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{1\text{-heteroaryl}}$ group is bonded to $-(CH_2)_{0\text{-}3}-$ by any ring atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_3 alkyl,

(2) $-CF_3$,

(3) -F, Cl, -Br, or –I,

(4) C_1-C_3 alkoxy,

(5) –O-CF_3,

(6) -NH_2,

(7) -OH, or

(8) -C≡N,

with the proviso that when n_1 is zero $R_{1\text{-heteroaryl}}$ is not bonded to the carbon chain by nitrogen, or

(VII) -$(CH_2)_{n1}$-($R_{1\text{-heterocycle}}$) where n_1 is as defined above and

$R_{1\text{-heterocycle}}$ is:

(A) morpholinyl,

(B) thiomorpholinyl,

(C) thiomorpholinyl S-oxide,

(D) thiomorpholinyl S,S-dioxide,

(E) piperazinyl,

(F) homopiperazinyl,

(G) pyrrolidinyl,

(H) pyrrolinyl,

(I) tetrahydropyranyl,

(J) piperidinyl,

(K) tetrahydrofuranyl, or

(L) tetrahydrothiophenyl,

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

(1) =O,

(2) C_1-C_3 alkyl,

(3) –CF_3,

(4) -F, Cl, -Br and –I,

(5) C_1-C_3 alkoxy,

(6) –O-CF_3,

(7) -NH_2,

(8) -OH, or

(9) -C≡N,

with the proviso that when n_1 is zero $R_{1\text{-heterocycle}}$ is not bonded to the carbon chain by nitrogen;

where R_2 is:

(I) -H,

(II) C_1-C_6 alkyl, or

(III) -$(CH_2)_{0-4}$-R_{2-1} where R_{2-1} is (C_3-C_6)cycloalkyl, $R_{1\text{-aryl}}$ or $R_{1\text{-heteroaryl}}$ where $R_{1\text{-aryl}}$ and $R_{1\text{-heteroaryl}}$ are as defined above,

where R_N is:

(I) R_{N-1}-X_N- where X_N is:

(A) –CO-,

(B) –SO_2-,

(C) -$(CR'R'')_{1-6}$ where R' and R" are the same or different and are –H or C_1-C_4 alkyl,

(D) –CO-$(CR'R'')_{1-6}$-X_{N-1} where X_{N-1} is –O-, -S- and –NR'R"- and where R' and R" are as defined above,

(E) a single bond;

where R_{N-1} is:

(A) $R_{N\text{-aryl}}$ where $R_{N\text{-aryl}}$ is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or -I,

(3) -OH,

(4) -NO_2,

(5) -CO-OH,

(6) -C≡N,

(7) -CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) -C_1-C_6 alkyl unsubstituted or substituted with one to three –F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e) -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-R_{N-4} where R_{N-4} is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-R_{N-5} where R_{N-5} is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0-2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) $-SO_2-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are as defined above,

(15) $-SO-(C_1-C_8$ alkyl),

(16) $-SO_2-(C_3-C_{12}$ alkyl),

(17) $-NH-CO-O-R_{N-5}$ where R_{N-5} is as defined above,

(18) $-NH-CO-N(C_1-C_3$ alkyl$)_2$,

(19) $-N-CS-N(C_1-C_3$ alkyl$)_2$,

(20) $-N(C_1-C_3$ alkyl$)-CO-R_{N-5}$ where R_{N-5} is as defined above,

(21) $-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(22) $-R_{N-4}$ where R_{N-4} is as defined above,

(23) $-O-CO-(C_1-C_6$ alkyl),

(24) $-O-CO-N(C_1-C_3$ alkyl$)_2$,

(25) $-O-CS-N(C_1-C_3$ alkyl$)_2$,

(26) $-O-(C_1-C_6$ alkyl),

(27) $-O-(C_2-C_5$ alkyl$)-COOH$,

(28) $-S-(C_1-C_6$ alkyl),

(29) C_1-C_6 alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F,

(30) $-O-(C_1-C_6$ alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 –F, or

(31) –O-ϕ,

(B) $-R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,

(DD) thiadiazolyl,

(EE) triazolyl,

(FF) tetrazolyl,

(GG) 1, 4-benzodioxan

(HH) purinyl,

(II) oxazolopyridinyl,

(JJ) imidazopyridinyl,

(KK) isothiazolyl,

(LL) naphthyridinyl,

(MM) cinnolinyl,

(NN) carbazolyl,

(OO) β-carbolinyl,

(PP) isochromanyl,

(QQ) chromanyl,

(RR) furazanyl,

(SS) tetrahydroisoquinoline,

(TT) isoindolinyl,

(UU) isobenzotetrahydrofuranyl,

(VV) isobenzotetrahydrothienyl,

(WW) isobenzothiophenyl,

(XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the $R_{N\text{-heteroaryl}}$ group is bonded by any atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{N\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

(1) C_1-C_6 alkyl,

(2) –F, -Cl, -Br, or - I,

(3) -OH,

(4) $-NO_2$,

(5) -CO-OH,

(6) -C≡N,

(7) $-CO-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are the same or different and are:

(a) -H,

(b) -C_1-C_6 alkyl unsubstituted or substituted with one

(i) -OH, or

(ii) $-NH_2$,

(c) -C_1-C_6 alkyl unsubstituted or substituted with 1, 2, or 3 –F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

(g) -C_1-C_6 alkenyl with one or two double bonds,

(h) -C_1-C_6 alkynyl with one or two triple bonds,

(i) -C_1-C_6 alkyl chain with one double bond and one triple bond,

(j) -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or

(k) -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) -CO-(C_3-C_{12} alkyl),

(9) -CO-(C_3-C_6 cycloalkyl),

(10) -CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(11) -CO-$R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(12) -CO-$R_{N\text{-}4}$ where $R_{N\text{-}4}$ is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C_1-C_3 alkyl,

(13) -CO-O-$R_{N\text{-}5}$ where $R_{N\text{-}5}$ is:

(a) C_1-C_6 alkyl, or

(b) -$(CH_2)_{0\text{-}2}$-($R_{1\text{-aryl}}$) where $R_{1\text{-aryl}}$ is as defined above,

(14) -SO_2-$NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined above,

(15) -SO-(C_1-C_8 alkyl),

(16) -SO_2-(C_3-C_{12} alkyl),

(17) -NH-CO-O-R_{N-5} where R_{N-5} is as defined above,

(18) -NH-CO-N(C_1-C_3 alkyl)$_2$,

(19) -N-CS-N(C_1-C_3 alkyl)$_2$,

(20) –N(C_1-C_3 alkyl)-CO-R_{N-5} where R_{N-5} is as defined above,

(21) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(22) -R_{N-4} where R_{N-4} is as defined above,

(23) –O-CO-(C_1-C_6 alkyl),

(24) -O-CO-N(C_1-C_3 alkyl)$_2$,

(25) -O-CS-N(C_1-C_3 alkyl)$_2$,

(26) -O-(C_1-C_6 alkyl),

(27) -O-(C_2-C_5 alkyl)-COOH, or

(28) -S-(C_1-C_6 alkyl),

(C) -$R_{N\text{-}aryl}$-$R_{N\text{-}aryl}$ where -$R_{N\text{-}aryl}$ is as defined above,

(D) -$R_{N\text{-}aryl}$-$R_{N\text{-}heteroaryl}$ where -$R_{N\text{-}aryl}$ and -$R_{N\text{-}heteroaryl}$ are as defined above,

(E) -$R_{N\text{-}heteroaryl}$-$R_{N\text{-}aryl}$ where -$R_{N\text{-}aryl}$ and -$R_{N\text{-}heteroaryl}$ are as defined above,

(F) -$R_{N\text{-}heteroaryl}$-$R_{N\text{-}heteroaryl}$ where $R_{N\text{-}heteroaryl}$ is as defined above,

(G) -$R_{N\text{-}aryl}$-O-$R_{N\text{-}aryl}$ where -$R_{N\text{-}aryl}$ is as defined above,

(H) -$R_{N\text{-}aryl}$-S-$R_{N\text{-}aryl}$ where -$R_{N\text{-}aryl}$ is as defined above,

(I) -$R_{N\text{-}heteroaryl}$-O-$R_{N\text{-}heteroaryl}$ where $R_{N\text{-}heteroaryl}$ is as defined above,

(J) -$R_{N\text{-}heteroaryl}$-S-$R_{N\text{-}heteroaryl}$ where $R_{N\text{-}heteroaryl}$ is as defined above,

(K) -$R_{N\text{-}aryl}$-CO-$R_{N\text{-}aryl}$ where -$R_{N\text{-}aryl}$ is as defined above,

(L) -$R_{N\text{-}aryl}$-CO-$R_{N\text{-}heteroaryl}$ where -$R_{N\text{-}aryl}$ and $R_{N\text{-}heteroaryl}$ are as defined above,

(M) -$R_{N\text{-}aryl}$-SO_2-$R_{N\text{-}aryl}$ where -$R_{N\text{-}aryl}$ is as defined above,

(N) -$R_{N\text{-heteroaryl}}$-CO-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(O) -$R_{N\text{-heteroaryl}}$-SO_2-$R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above,

(P) –$R_{N\text{-aryl}}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-aryl}}$ is as defined above,

(Q) –$R_{N\text{-aryl}}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-aryl}}$ is as defined above,

(R) –$R_{N\text{-heteroaryl}}$-O-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above, or

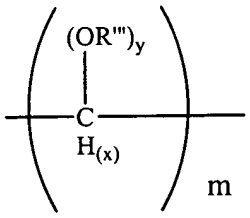
(S) –$R_{N\text{-heteroaryl}}$-S-(C_1-C_8 alkyl)-ϕ where $R_{N\text{-heteroaryl}}$ is as defined above,

(II) A-X_N- where X_N is –CO-,

wherein A is

(A) -T-E-$(Q)_{m'}$,

(1) where -T is



where

(a) x =1 when y = 1 and x = 2 when y = 0,

(b) m is 0, 1, 2 or 3,

(c) the values of x and y vary independently on each carbon when m is 2 and 3, and

(d) R''' varies independently on each carbon and is H, (C_1-C_2) alkyl, phenyl, or phenyl(C_1-C_3)alkyl;

(2) -E is

(a) C_1-C_5 alkyl, but only if m' does not equal 0,

(b) methylthioxy(C_2-C_4)alkyl,

(c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,

(f) biphenyl,

(g) diphenyl ether,

(h) diphenylketone,

(i) phenyl(C_1-C_8)alkyloxyphenyl, or

(j) C_1-C_6 alkoxy;

(3) -Q is

(a) C_1-C_3 alkyl,

(b) C_1-C_3 alkoxy,

(c) C_1-C_3 alkylthioxy,

(d) C_1-C_6 alkylacylamino,

(e) C_1-C_6 alkylacyloxy,

(f) amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary amino moieties),

(g) C_1-C_6 alkylamino

(h) phenylamino,

(i) carbamyl (including C_1-C_6 alkyl and phenyl amides and esters),

(j) carboxyl (including C_1-C_6 alkyl and phenyl esters),

(k) carboxy(C_2-C_5)alkoxy,

(l) carboxy(C_2-C5)alkylthioxy,

(m) heterocyclylacyl,

(n) heteroarylacyl, or

(o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) -$E(Q)_{m''}$ wherein E and -Q are as defined as above and m'' is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

(III) –CO-(C_1-C_6 alkyl) where alkyl is unsubstituted or substituted with one or two:

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} is the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(IV) –CO-(C_1-C_3 alkyl)-O-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(V) –CO-(C_1-C_3 alkyl)-S-(C_1-C_3 alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) –CO-O-R_{N-8} where R_{N-8} is –H, C_1-C_6 alkyl or -ϕ,

(E) –CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,

(K) -$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$ where the R_{N-8} are the same or different and are as defined above, or

(O) -O-(C_1-C_5 alkyl)-COOH,

(VI) –CO-CH(-$(CH_2)_{0-2}$-O-R_{N-10})-$(CH_2)_{0-2}$-R_{N-aryl}/$R_{N-heteroaryl}$) where R_{N-aryl} and $R_{N-heteroaryl}$ are as defined above, where R_{N-10} is:

(A) –H,

(B) C_1-C_6 alkyl,

(C) C_3-C_7 cycloalkyl,

(D) C_2-C_6 alkenyl with one double bond,

(E) C_2-C_6 alkynyl with one triple bond,

(F) R_{1-aryl} where R_{1-aryl} is as defined above, or

(G) $R_{N-heteroaryl}$ where $R_{N-heteroaryl}$ is as defined above;

where B is -O-, -NH-, or -N(C_1-C_6 alkyl)-;

where R_C is:

(I) -(C_1-C_{10})alkyl-K_{1-3} in which:

(A) the alkyl chain is unsubstituted or substituted with one –OH,

(B) the alkyl chain is unsubstituted or substituted with one C_1-C_6 alkoxy unsubstituted or substituted with 1-5 -F,

(C) the alkyl chain is unsubstituted or substituted with one –O-ϕ,

(D) the alkyl chain is unsubstituted or substituted with 1-5 –F,

(E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

(1) H,

(2) C_1-C_3 alkyl,

(3) C_1-C_3 alkoxy,

(4) C_1-C_3 alkylthioxy,

(5) C_1-C_6 alkylacylamino,

(6) C_1-C_6 alkylacyloxy,

(7) amido

(8) C_1-C_6 alkylamino

(9) phenylamino,

(10) carbamyl

(11) carboxyl

(12) carboxy(C_2-C_5)alkoxy,

(13) carboxy(C_2-C5)alkylthioxy,

(14) heterocyclylacyl,

(15) heteroarylacyl,

(16) amino unsubstituted or substituted with C_1-C_6 alkyl,

(17) hydroxyl, or

(18) carboxyl methyl ester;

(II)-$(CH_2)_{0-3}$-J-[(-$(CH_2)_{0-3}$-K]$_{1-3}$ where K is as defined above and J is:

(A) a 5 to 7 atom monocyclic aryl group,

(B) a 8 to 12 atom multicyclic aryl group,

(C) a 5 to 7 atom heterocyclic group,

(D) a 8 to 12 atom multicyclic heterocyclic group, or

(E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -$(CH_2)_{0-3}$-(C_3-C_7) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

(A) C_1-C_3 alkyl unsubstituted or substituted with 1, 2, 3, or 4 –F, -Cl, -Br, or -I,

(B) -CO-OH,

(C) -CO-O-(C_1-C_4 alkyl),

(D) -OH, or

(E) C_1-C_6 alkoxy,

(IV) $-(CH_2)_{2-6}$-OH,

(V) $-(CR_{C-x}R_{C-y})_{0-4}$-R_{C-aryl} where R_{C-x} and R_{C-y} are –H, C_1-C_4 alkyl and ϕ- and R_{C-aryl} is the same as R_{N-aryl},

(VI) $-(CH_2)_{0-4}$-$R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) isoxazolyl,

(Q) pyrazolyl,

(R) indolizinyl,

(S) indazolyl,

(T) benzothiazolyl,

(U) benzimidazolyl,

(V) benzofuranyl,

(W) furanyl,

(X) thienyl,

(Y) pyrrolyl,

(Z) oxadiazolyl,

(AA) thiadiazolyl,

(BB) triazolyl,

(CC) tetrazolyl,

(DD) 1, 4-benzodioxan

(EE) purinyl,

(FF) oxazolopyridinyl,

(GG) imidazopyridinyl,

(HH) isothiazolyl,

(II) naphthyridinyl,

(JJ) cinnolinyl,

(KK) carbazolyl,

(LL) β-carbolinyl,

(MM) isochromanyl,

(NN) chromanyl,

(OO) furazanyl,

(PP) tetrahydroisoquinoline,

(QQ) isoindolinyl,

(RR) isobenzotetrahydrofuranyl,

(SS) isobenzotetrahydrothienyl,

(TT) isobenzothiophenyl,

(UU) benzoxazolyl, or

(VV) pyridopyridinyl,

(VII) $-(CH_2)_{0-4}-R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is the same as $R_{1\text{-heterocycle}}$,

(VIII) $-C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3}$ where R_{C-1} and R_{C-2} are the same or different and are:

(A) -H,

(B) $-C_1-C_6$ alkyl,

(C) $-(C_1-C_4$ alkyl$)-R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above for $R_{1\text{-aryl}}$,

(D) $-(C_1-C_4$ alkyl$)-R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above,

(E) -(C_1-C_4 alkyl)-$R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(F) –$R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above,

(G) –$R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(H) –$(CH_2)_{1\text{-}4}$-OH,

(I) -$(CH_2)_{1\text{-}4}$-$R_{C\text{-}4}$-$(CH_2)_{1\text{-}4}$-$R_{C'\text{-aryl}}$ where $R_{C\text{-}4}$ is –O-, -S-, -NH- or –$NHR_{C\text{-}5}$- where $R_{C\text{-}5}$ is C_1-C_6 alkyl, and where $R_{C'\text{-aryl}}$ is as defined above,

(J) -$(CH_2)_{1\text{-}4}$-$R_{C\text{-}4}$-$(CH_2)_{1\text{-}4}$-$R_{C\text{-heteroaryl}}$ where $R_{C\text{-}4}$ and $R_{C\text{-heteroaryl}}$ are as defined above, or

(K) –$R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above,

and where $R_{C\text{-}3}$ is:

(A) -H,

(B) -C_1-C_6 alkyl,

(C) –$R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above,

(D) –$R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above,

(E) –$R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(F) -(C_1-C_4 alkyl)-$R_{C'\text{-aryl}}$ where $R_{C'\text{-aryl}}$ is as defined above,

(G) -(C_1-C_4 alkyl)-$R_{C\text{-heteroaryl}}$ where $R_{C\text{-heteroaryl}}$ is as defined above, or

(H) -(C_1-C_4 alkyl)-$R_{C\text{-heterocycle}}$ where $R_{C\text{-heterocycle}}$ is as defined above,

(IX) -$CH(\phi)_2$,

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

(A) C_1-C_3 alkyl,

(B) –CF_3,

(C) -F, Cl, -Br and –I,

(D) C_1-C_3 alkoxy,

(E) -OCF_3,

(F) $-NH_2$,

(G) -OH, or

(H) $-C\equiv N$,

(XI) $-CH_2-C\equiv CH$;

(XII) $-(CH_2)_{0-1}-CHR_{C-5}-(CH_2)_{0-1}-\phi$ where R_{C-5} is:

(A) –OH, or

(B)$-CH_2-OH$;

(XIII) $-CH(-\phi)-CO-O(C_1-C_3$ alkyl);

(XIV) $-CH(-CH_2-OH)-CH(-OH)-\phi-NO_2$;

(XV) $-(CH_2)_2-O-(CH_2)_2-OH$;

(XVI) $-CH_2-NH-CH_2-CH(-O-CH_2-CH_3)_2$;

(XVII) $-(C_2-C_8)$ alkynyl; or

(XVIII) –H; or a pharmaceutically acceptable salt thereof.

in a reaction mixture under conditions suitable for the production of said complex.

62. The method of claim 61, where said exposing is *in vitro.*

63. The method of claim 61, wherein said reaction mixture is a cell.